The Journal of Pediatrics

VOL. 14 JUNE, 1939 NO. 6

Original Communications

SEPSIS OF THE NEWBORN INFANT

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THERE has been a sharp drop in the general morbidity and mortality rate in infancy and childhood during the last fifty years. The rate during the first month of life, however, has remained almost stationary; the decrease having occurred in the age brackets above the neonatal period. According to the U. S. Bureau of the Census for 1935, 32 deaths per 1,000 live births occurred during the first month, in comparison with 23 deaths per 1,000 in the succeeding eleven months of the first year. Of the 32 deaths during the first month, 25 are attributed to natal and prenatal causes. Prematurity, congenital malformations, birth injuries, syphilis, tetanus, and sepsis are among the prominent causes of death in this period. The death rate from prematurity, birth injuries, syphilis, and tetanus has been materially reduced by improvements in technique and prenatal care. Deaths due to congenital malformations are subject to reduction in rate with improvement in surgical technique. There is a minimum, however, in each of these classifications below which reduction is unlikely. The incidence of deaths from sepsis has not been reduced, but on the contrary epidemics, apparently of sepsis, have occurred with increasing frequency in the neonatal group in hospitals previously free from infections. Our efforts, therefore, should be directed particularly toward the control of sepsis in the newborn infant. In the United States nursery infections have occurred from coast to coast, and similar epidemics have been reported from several foreign countries. Some institutions have had recurrences.

The disease has been ascribed to different microorganisms, by various observers, and, because of the prominence of diarrhea as a symptom, most authors have classified these epidemics as infectious diarrhea. However, a lack of clinical data preceding the onset of the diarrhea in the cases reported makes it difficult for a critical reviewer to differentiate these from epidemics of "sepsis in the newborn in-

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fant." The fact that the newborn babies are known to have low resistance to pyogenic organisms and that such invasion is often accompanied by frequent stools makes an assumption of "sepsis" as a primary disease seem more logical than a diagnosis of primary diarrhea. This differentiation is important since control of such epidemics must be based upon a knowledge of the medium through which the infection enters a nursery or is transmitted from infant to infant. Contact, air-borne and food-borne infections are all possible, and each may be accompanied by sepsis manifesting itself by diarrhea.

The atria of infection in the newborn infants are not only the gastrointestinal but also the skin and respiratory tracts. Diarrhea follows primary infections of the gastrointestinal and upper respiratory tracts with equal frequency. It not infrequently follows sepsis with primary infection in the skin, subcutaneous tissue, or umbilical vein.

Several epidemics of "sepsis" have occurred in the newborn infants under our observation. Individual infants in each of these epidemics have had diarrhea, but bronchopneumonia occurred in several and endocarditis in one, without evidence of intestinal irritation.

The clinical histories and laboratory reports of 27 patients seen in an epidemic observed in December, 1937, at Cook County Hospital, are presented. The necropsy reports of the 7 who died are included. The epidemic occurred in the nursery of Ward 51 assigned to normal obstetrics where there were 168 births and in Ward 41 devoted to pregnant women with syphilis, gonorrhea, and acute infections, in which there were 34 live and 5 stillbirths. A contiguous Ward 50 assigned to operative and complicated obstetrics, with 102 live and seven stillbirths, was unaffected.

To recapitulate, twenty-seven infants showed septic symptoms when 277 other newborn infants in the same wards were unaffected.

The clinical picture at the onset of the disease was similar in all cases. Loss of appetite and failure to gain weight were the prominent symptoms. They preceded any change in the number, consistency, and color of the stools by several days. The early loss of weight was not explainable as a result of vomiting or diarrhea. About the third day after onset the stools of some became softer and in some instances, liquid. The color changed to greenish yellow with the occasional presence of mucus. The average number of stools per day was five with the minimum of three and the maximum of eight. No rise of temperature occurred during the first three days, after which a rise to 100° F. occurred in most instances. Several, developing bronchopneumonia, had a higher temperature during this second phase of the disease.

Listlessness was present during the first phase of the disease and continued throughout its entire course. The children seemed to be in no discomfort but had to be urged to take food. Their general ap-

pearance seemed to be that of an intoxication rather than of a localized infection.

From the fourth day on the children could be divided into five groups symptomatically:

A. A group, which following the period of lethargy and weight loss, went on to uneventful recovery without developing respiratory or intestinal symptoms.

B. A group in which diarrhea was the prominent symptom. All recovered.

C. A group with stationary or slight increase in weight, mild gastrointestinal disturbance (frequent and soft stools), and gradually disappearing lethargy. These were improved at the end of a week and completely recovered at the end of the second week.

D. A group with mild bronchopneumonia, temperature rising to 102°-104° F., with recovery at the end of ten to fourteen days.

E. A group with severe intoxication with or without symptoms of bronchopneumonia or gastrointestinal disturbance. All died.

As the patient improved, lethargy became less, food was taken more readily, stools became less frequent and more normal, temperature approached normal, and a slow steady gain in weight began.

CASE HISTORIES

Ward 41 (Venereal Disease and Other Infections)

CASE 1.—Baby of L. Sc., born Dec. 10, 1937; weight, 2,520 gm.; normal delivery, eight months' gestation; initial feeding, evaporated milk mixture; mother had a doubtful Kahn test. Considerable mucus was present in the infant's pharynx at birth and after its aspiration, an ampoule of alpha lobeline was administered.

Symptoms.—On Dec. 13, 1937, a diffuse erythema with brawny induration and sharply demarcated and elevated borders appeared, involving the left side of the head, face, chin, and shoulder. It was diagnosed erysipelas, and baby was transferred to the Contagious Division. Prontylin therapy was instituted, and the lesion cleared in three days, leaving a localizing abscess of the upper outer third of the left arm.

Course.—Infant transferred to Children's Division, Dec. 16, 1937. On Dec. 17, 1937, liquid stools were first noted, after which there were four to six soft or liquid stools daily.

Laboratory Findings.—Stool cultures yielded *B. pyocyaneus.*

Diagnosis.—Sepsis.

Result.—Patient expired Dec. 27, 1937.

Autopsy Findings.—Multiple abscesses of the scalp and left shoulder region; focal bronchopneumonia; cloudy swelling and fatty changes of the liver and kidneys; infectious hyperplasia of the spleen.

Post-Mortem Bacteriology.—Aerobic and anaerobic cultures revealed *B. coli* in the heart blood; *B. coli* and *B. mucosus capsulatus* in the colon; *B. mucosus capsulatus* and *B. coli* in the ileum.

CASE 2.—Baby of H. E., born Dec. 12, 1937; weight, 2,700 gm.; normal delivery; initial feeding, evaporated milk mixture; mother's Wassermann, positive.

Symptoms.—Persistent loss of weight, slight elevation of temperature (99° F., axillary) and loose stools Dec. 20, 1937.

Course.—Transferred to Children's Division Dec. 20, 1937. There were three to four stools daily, some liquid.

Laboratory Findings.—Stool cultures yielded *B. pyocyaneus.*

Diagnosis.—Bronchopneumonia with secondary diarrhea.

Result.—Patient expired Dec. 23, 1937.

Autopsy Findings.—Focal and confluent bronchopneumonia; parenchymatous degeneration of the liver, kidneys, and myocardium; malnutrition and dehydration; hyperplasia and hyperemia of Peyer's patches.

Post-Mortem Bacteriology.—Mixed growth from intestine containing *B. pyocyaneus.*

CASE 3.—Baby of D. W., born Dec. 10, 1937; weight, 3,015 gm.; normal delivery; initial feeding, evaporated milk mixture; mother, two-plus Kahn. X-ray reported no evidence of syphilis in infant's long bones.

Symptoms.—On Dec. 19, 1937, the buttocks were excoriated and on Dec. 20, 1937, the child became listless, developed grunting respirations, abdominal distention, and a temperature of 95.4° F. rectally.

Course.—Transferred to Children's Division, Dec. 20, 1937.

Laboratory Findings.—No stool cultures.

Diagnosis.—Bronchopneumonia.

Result.—Death Dec. 20, 1937—four hours after transfer.

Autopsy Findings.—Diffuse bronchopneumonia; infectious hyperplasia of the spleen; passive congestion of the liver, spleen, and kidneys; edema and hyperemia of the brain.

Post-Mortem Bacteriology.—No cultures taken.

CASE 4.—Baby of E. P., born Dec. 12, 1937; weight, 3,105 gm.; normal delivery; initial feeding, evaporated milk mixture; mother had doubtful Kahn.

Symptoms.—Infant sneezed, had sniffles, temperature 101° F. rectally, and a watery stool.

Course.—Transferred to the Children's Division Dec. 21, 1937. There were three to seven stools daily, several watery.

Laboratory Findings.—Stool cultures were negative for the colon typhoid, salmonella group, and *B. pyocyaneus.*

Diagnosis.—Infection of upper respiratory tract, with secondary diarrhea.

Result.—Discharged cured, Jan. 22, 1938.

CASE 5.—Baby of P. H., born Dec. 4, 1937; weight, 2,940 gm.; normal delivery; initial feeding, evaporated milk mixture; mother had a four-plus Wassermann; x-ray of the infant's long bones was reported negative for syphilis.

Course.—Discharged as normal newborn infant, Dec. 13, 1937. Admitted to Children's Division Dec. 26, 1937.

Symptoms.—Difficult respirations and subsequently four to five loose green stools daily.

Laboratory Findings.—No cultures done.

Diagnosis.—Bronchopneumonia with secondary diarrhea.

Result.—Death ten hours after admission.

Autopsy Findings.—Catarrhal enterocolitis; focal bronchopneumonia; anemia and parenchymatous degeneration of the myocardium, liver, and kidneys.

Post-Mortem Bacteriology.—*B. mucosus capsulatus* from the heart blood; *B. mucosus capsulatus* predominating with *B. coli* and *B. proteus* in the bile; *B. mucosus capsulatus* predominating with *B. coli, Str. viridans* and *Staph. albus* in the colon; *B. mucosus capsulatus* predominating with *B. coli* and *B. proteus* in the ileum; *B. proteus, B. coli, B. mucosus capsulatus* and *Str. viridans* from the peritoneal fluid.

CASE 6.—Baby of E. J., born Dec. 17, 1937; weight, 2,840 gm.; normal delivery; initial feeding, evaporated milk mixture; mother was suspected of syphilis, but Kahn test was negative.

Symptoms.—On Dec. 24, 1937, sniffling, refusal of the formula, temperature 99.6° F. rectally, and a yellowish loose stool occurred.

Course.—Transferred to Children's Division. There were four to ten stools daily, many liquid.

Laboratory Findings.—Stool cultures negative for the colon typhoid, salmonella group and *B. pyocyaneus.*

Diagnosis.—Infection of the upper respiratory tract, with secondary diarrhea.

Result.—Discharged cured Jan. 22, 1938.

CASE 7.—Baby of A. M., born Nov. 25, 1937; weight 2,880 gm.; normal delivery; initial feeding, evaporated milk mixture; mother suspected of miliary tuberculosis.

Symptoms.—Several slightly watery stools Dec. 28, 1937.

Course.—Infant remained in ward nursery for newborn because of mother's tuberculosis, and was transferred to Children's Division Dec. 28, 1937, with three to six stools daily, occasionally liquid. No elevation of temperature, but later reached 102° F. (axillary).

Laboratory Findings.—Stool cultures, *B. pyocyaneus.*

Diagnosis.—Primary diarrhea.

Result.—Discharged cured Jan. 31, 1938.

CASE 8.—Baby of A. S., born Dec. 23, 1937; weight, 2,900 gm.; normal delivery; initial feeding, evaporated milk mixture; mother diagnosed as having gonorrheal vaginitis.

Symptoms.—None; infant transferred to Children's Division on Dec. 28, 1937, because of closure of the ward nursery.

Course.—Loose stools, temperature 100° F. (axillary), Dec. 29, 1937. Septic temperature reaching 102° F. (axillary), with diarrhea until death.

Laboratory Findings.—Stool cultures negative for the colon typhoid, salmonella group, and *B. pyocyaneus.*

Diagnosis.—Sepsis of newborn.

Result.—Patient expired Jan. 7, 1938.

Autopsy Findings.—Mural endocarditis and verrucous endocarditis of the mitral valves; fibrinous pericarditis; multiple abscesses of both kidneys and myocardium; acute hemorrhagic enterocolitis; passive congestion of all organs.

Post-Mortem Bacteriology.—*Staph. aureus* from the heart blood, staphylococci in the pericardial fluid; *Staph. aureus* and *B. coli*, in the bile; *B. coli, Staph. aureus, B. aerogenes* and *B. proteus* in the colon and ileum.

CASE 9.—Baby of M. O., born Nov. 3, 1937; weight, 3,900 gm.; normal delivery; initial feeding, boiled milk mixture; mother had scabies.

Symptoms.—None; infant transferred to Children's Division on Dec. 28, 1937, because of closure of ward nursery.

Course.—On Dec. 29, 1937, five stools, one liquid. Thereafter, an occasional liquid stool. Temperature normal throughout.

Laboratory Findings.—Stool cultures yielded *B. pyocyaneus.*

Diagnosis.—Diarrhea.

Result.—Discharged cured Jan. 22, 1938.

CASE 10.—Baby of J. H., born Nov. 25, 1937; weight, 3,065 gm.; normal delivery; initial feeding, raw breast milk; mother had a positive Kahn test.

Course.—Discharged normal newborn Dec. 27, 1937. Admitted to Children's Division Dec. 29, 1937.

Symptoms.—Watery bowel movements, no elevation of temperature, two to five stools daily, occasionally liquid.

Laboratory Findings.—Stool cultures were negative for the colon typhoid, salmonella group, and *B. pyocyaneus.*

Diagnosis.—Diarrhea.

Result.—Discharged cured Jan. 19, 1938.

CASE 11.—Baby of F. P., born Dec. 16, 1937; weight, 3,195 gm.; normal delivery; initial feeding, evaporated milk mixture; mother had urticaria and an infection of the upper respiratory tract.

Course.—Discharged as normal newborn infant Dec. 24, 1937. Admitted to Children's Division Dec. 30, 1937.

Symptoms.—History of greenish liquid stools for preceding five days. In hospital, three to five stools daily, occasionally liquid.

Laboratory Findings.—Stool cultures were negative once and positive once for *B. pyocyaneus.*

Diagnosis.—Diarrhea.

Result.—Discharged cured Jan. 20, 1938.

Ward 51 (Normal Obstetrics)

CASE 12.—Baby of E. O., born Nov. 29, 1937; weight, 4,080 gm.; normal delivery; initial feeding, at breast.

Course.—Transferred to Children's Division Dec. 6, 1937, three to six stools daily, yellowish green color, occasionally semiliquid. Discharged cured Jan. 1, 1938. Readmitted to Children's Division Jan. 9, 1938, three greenish, watery stools daily for preceding three days.

Symptoms.—On Dec. 6, 1937, elevation of temperature 100.6° F. (rectally) and several loose stools. On readmission, stools again were liquid.

Laboratory Findings.—Stool cultures in both instances negative for colon typhoid, salmonella group, and *B. pyocyaneus.*

Diagnosis.—Infection of the upper respiratory tract with secondary diarrhea.

Result.—Discharged cured Jan. 1, 1938. Second discharge, cured, Feb. 1, 1938.

CASE 13.—Baby of C. D., born Dec. 3, 1937; weight, 2,940 gm.; normal delivery; initial feeding, at breast.

Course.—Discharged as normal newborn infant, Dec. 13, 1937. Admitted to Children's Division Dec. 17, 1937.

Symptoms.—On Dec. 16, 1937, nasal discharge, sneezing, drainage from the umbilicus, loose watery stools occurred. Temperature 107° F. (axillary).

Laboratory Findings.—Stool cultures negative for the colon typhoid, salmonella group, and *B. pyocyaneus.*

Diagnosis.—Infection of the upper respiratory tract; umbilical sepsis; secondary diarrhea.

Result.—Patient expired Jan. 2, 1938.

Autopsy Findings.—Hemorrhagic bronchopneumonia; icterus gravis neonatorum; anemia and degeneration of parenchymatous organs.

Post-Mortem Bacteriology.—Cultures from heart's blood, *Str. viridans;* from intestine, *B. coli* and *Staph. albus.*

CASE 14.—Baby of H. P., born Dec. 5, 1937; weight, 2,858 gm.; normal delivery; initial feeding, at breast.

Symptoms.—Jaundice Dec. 13, 1937, persistent; failure to gain weight.

Course.—Transferred to Children's Division Dec. 18, 1937. Loose stools appeared next day, yellowish green, three to six daily, occasionally liquid.

Laboratory Findings.—Stool cultures yielded *B. enteritides.*

Diagnosis.—Sepsis of newborn.

Result.—Discharged cured Jan. 8, 1938.

CASE 15.—Baby of T. S., born Dec. 17, 1937; weight, 3,488 gm.; normal delivery; initial feeding, at breast. Mother diagnosed as having scarlet fever Dec. 18, 1937, and transferred to Contagious Division.

Symptoms.—Temperature 101.8° F. rectally, Dec. 21, 1937.

Course.—Transferred to Children's Division Dec. 21, 1937.

Laboratory Findings.—No cultures done.

Diagnosis.—Bronchopneumonia and sepsis.

Result.—Patient expired Dec. 23, 1937.

Autopsy Findings.—Bronchopneumonia.

Post-Mortem Bacteriology.—Cultures, intestinal contents; *B. coli, B. aerogenes, Staph. albus* and *Str. viridans.*

CASE 16.—Baby of J. M., born Dec. 15, 1937; weight, 3,165 gm.; normal delivery; initial feeding, at breast.

Symptoms.—Temperature 101° F. (axillary), mass in left upper quadrant Dec. 19, 1937. Stools curded and dyspeptic.

Course.—Transferred to Children's Division Dec. 20, 1937. Liquid stool Dec. 22, 1937, green-yellow, soft, three to four daily.

Laboratory Findings.—Stool cultures yielded *B. enteritides.*

Diagnosis.—Splenomegaly and sepsis of newborn.

Result.—Discharged cured Jan. 19, 1938.

CASE 17.—Baby of A. K., born Dec. 8, 1937; weight, 2,670 gm.; normal delivery; initial feeding, at breast. Condition fair at birth, placed in ward nursery incubator.

Symptoms.—Persistent jaundice and marked anemia.

Course.—Transferred to Children's Division Dec. 17, 1937. One liquid stool, Dec. 20, 1937, with four to five liquid stools Dec. 23, 1937.

Laboratory Findings.—Stool cultures yielded *B. enteritides.*

Diagnosis.—Marked physiologic jaundice and sepsis of the newborn.

Result.—Discharged cured Jan. 26, 1938.

CASE 18.—Baby of C. Y., born Dec. 18, 1937; weight, 2,865 gm.; normal delivery; initial feeding, skimmed lactic acid milk.

Symptoms.—General condition poor at birth, limpness, cyanosis, and grunting respirations. Marked jaundice, bleeding from the bladder and umbilical cord appeared four hours after birth.

Course.—Transferred to Children's Division several hours after birth. Mucus noted in stool Dec. 19, 1937, liquid stools Dec. 22, 1937, greenish yellow, five to seven daily.

Laboratory Findings.—Stool cultures negative for the colon typhoid, salmonella group, and *B. pyocyaneus.* Icteric index initially 90, dropped to 15.

Diagnosis.—Suspected erythroblastosis fetalis.

Result.—Discharged cured, Jan. 26, 1938.

CASE 19.—Baby of H. B.; born Dec. 13, 1937; weight, 2,790 gm.; frank breech presentation; initial feeding, raw breast milk.

Symptoms.—Jaundice appeared Dec. 23, 1937; and became exaggerated.

Course.—Placed in isolation nursery Dec. 23, 1937, mucoid stool, Dec. 24, 1937. green watery stool, Dec. 25, 1937. Transferred to Children's Division on latter date. There were three to six stools daily, some liquid.

Laboratory Findings.—Stool cultures negative for the colon typhoid, salmonella group and *B. pyocyaneus.*

Diagnosis.—Physiologic jaundice and sepsis of newborn.

Result.—Discharged cured, Jan. 18, 1938.

CASE 20.—Baby of E. B., born Dec. 15, 1937; weight, 3,525 gm.; normal delivery; initial feeding, at breast.

Symptoms.—Two pustules noted in right groin Dec. 21, 1937.

Course.—More lesions of similar character subsequently and watery stools Dec. 25, 1937. Infant transferred to Children's Division on that date. There were two to six stools daily, semiliquid and sometimes curded.

Laboratory Findings.—Stool cultures negative for colon typhoid, salmonella group, and *B. pyocyaneus.*

Diagnosis.—Impetigo and sepsis of the newborn.

Result.—Discharged cured Jan. 26, 1938.

CASE 21.—Baby of R. G., born Nov. 13, 1937; weight, 3,180 gm.; normal delivery; initial feeding, evaporated milk mixture.

Symptoms.—Marked bleeding from the cord several hours after birth. Jaundice, cyanosis, general condition poor.

Course.—Whole blood (15 c.c.) given intramuscularly. Transferred to Children's Division, Nov. 14, 1937. On Dec. 21, 1937, two semiliquid stools and after Dec. 24, 1937, three to five liquid stools daily.

Laboratory Findings.—Stool cultures yielded *B. pyocyaneus.* Icteric index 180 initially, dropped to 15.

Diagnosis.—Marked physiologic jaundice and sepsis of newborn.

Result.—Discharged cured Jan. 19, 1938.

CASE 22.—Baby of M. S., born Dec. 19, 1937; weight, 3,210 gm.; normal delivery; initial feeding, at breast.

Symptoms.—Several liquid stools Dec. 25, 1937.

Course.—Transferred to Children's Division Dec. 26, 1937. Semiliquid and liquid greenish yellow stools, four to six daily.

Laboratory Findings.—Stool cultures yielded *B. pyocyaneus.*

Diagnosis.—Diarrhea.

Result.—Discharged cured Jan. 27, 1938.

CASE 23.—Baby of P. P., born Dec. 18, 1937; weight, 2,805 gm.; normal delivery; initial feeding, at breast.

Symptoms.—Redness and swelling of the left lower eyelid Dec. 24, 1937.

Course.—Transferred to Children's Division Dec. 24, 1937; green semiliquid stools Dec. 27, 1937, thereafter, three to six loose stools daily.

Laboratory Findings.—Stool cultures negative for the colon typhoid, salmonella group, and *B. pyocyaneus.*

Diagnosis.—Dacryocystitis and sepsis of newborn.

Result.—Discharged cured Jan. 25, 1938.

CASE 24.—Baby of L. Sa., born Dec. 19, 1937; weight, 3,210 gm.; normal delivery; initial feeding, at breast.

Symptoms.—Temperature 100.4° F. (axillary), regurgitation of formula, loose stool Dec. 26, 1937. Liquid stool Dec. 27, 1937.

Course.—Transferred to Children's Division Dec. 27, 1937.

Laboratory Findings.—Stool cultures negative for the colon typhoid, salmonella group, and *B. pyocyaneus.*

Diagnosis.—Sepsis of newborn.

Result.—Discharged cured Feb. 1, 1938.

CASE 25.—Baby of B. W., born Dec. 4, 1937; weight, 2,615 gm.; normal delivery; initial feeding, at breast.

Course.—Discharged normal newborn Dec. 11, 1937. Admitted to Children's Division Dec. 31, 1937.

Symptoms.—Watery stools, two to four daily for preceding four days.

Laboratory Findings.—Stool cultures negative for the colon typhoid, salmonella group, *B. pyocyaneus.*

Diagnosis.—Diarrhea.

Result.—Discharged cured Jan. 19, 1938.

CASE 26.—Baby of M. de M., born Dec. 19, 1937; weight, 3,630 gm.; normal delivery; initial feeding, at breast.

Course.—Discharged normal newborn Dec. 27, 1937. Admitted to Children's Division Jan. 2, 1938.

Symptoms.—Yellowish mucous stools, four to six daily for preceding five days. Redness of eyes for same period.

Laboratory Findings.—Successive cultures yielded a different microorganism each time—*B. enteritides, B. pyocyaneus, B. coli.* Smears from the eye were negative for pathogenic organisms.

Diagnosis.—Bilateral conjunctivitis and secondary diarrhea.

Result.—Discharged cured Jan. 27, 1938.

CASE 27.—Baby of A. P., born Dec. 24, 1937; weight, 3,390 gm.; normal delivery; initial feeding, at breast.

Course.—Discharged normal newborn Jan. 3, 1938. Admitted to Children's Division eight hours later.

Symptoms.—Yellowish green liquid stools, three to six daily. Temperature 104° F. (axillary). Diffuse maculopapular eruption and bilateral conjunctivitis noted Jan. 5, 1938.

Laboratory Findings.—Stool cultures negative for the colon typhoid, salmonella group, and *B. pyocyaneus.* Eye smears negative for pathogenic organisms.

Diagnosis.—Sepsis of the newborn and bilateral conjunctivitis.

Result.—Discharged cured Jan. 27, 1938.

A survey was made of all potential foci from which the epidemic might have originated. It was found that the attending staff, five obstetricians and five associates, served the three wards as called upon for delivery. Patients were delivered and visited in all wards by all members of the staff. A resident was assigned to each ward; those of Ward 50 (operative) and of Ward 51 (normal obstetrics) relieved each other every second night by assuming both services. The resident on Ward 41 did not exchange services with either of the other

TABLE I

DIET, TREATMENT AND RESULTS

NAME	FORMULAS							TREATMENT					RESULT
	N.B. NUR.		PEDIATRIC WARD										
WARD 41	BR.	ART.	R.B.M.	B.B.M.	S.L.A.M.	P.P.M.	EVAP.	CLYSIS.	INT. VEN.	H & D	D & S	B.T.	
M. O.	–	+	+	–	+	–	–	+	–	+	–	–	Cured
A. M.	–	+	+	–	+	–	–	–	–	–	–	–	Cured
J. H.	–	+	+	–	+	–	–	+	–	+	–	–	Cured
P. H.	–	+	–	–	–	–	–	+	–	+	–	–	Death
L. Sc.	–	+	–	+	–	–	+	+	–	+	–	–	Death
D. W.	–	+	–	–	–	–	–	–	–	–	–	–	Death
H. E.	–	+	–	+	+	–	–	+	–	+	–	–	Death
E. P.	–	+	+	–	+	–	–	+	+	+	–	–	Cured
F. P.	–	+	–	–	–	+	–	+	–	+	–	+	Cured
E. J.	–	+	+	–	+	–	–	+	–	+	–	–	Cured
A. S.	–	+	+	–	+	–	–	–	+	+	–	+	Death
WARD 51													
R. G.	–	–	–	–	–	–	+	+	–	+	–	+	Cured
E. D.	+	+	+	–	+	–	–	+	–	+	–	–	Cured
C. D.	+	+	–	–	–	+	–	–	+	–	+	+	Death
B. W.	+	–	–	–	–	+	–	+	–	+	–	–	Cured
H. P.	+	+	–	–	+	–	–	+	–	+	–	–	Cured
A. K.	+	+	+	–	+	–	–	+	–	+	–	+	Cured
H. B.	+	+	+	–	+	–	–	+	–	+	–	–	Cured
F. B.	+	+	+	–	+	–	–	–	–	–	–	–	Cured
J. M.	+	–	–	+	+	–	–	+	–	+	–	–	Cured
T. S.	+	+	–	–	+	–	–	+	–	+	–	–	Death
P. P.	+	–	+	–	+	–	–	–	–	–	–	–	Cured
C. Y.	–	–	+	–	+	–	–	+	–	+	–	+	Cured
M. de M.	+	+	+	–	+	–	–	–	–	–	–	–	Cured
L. Sa.	+	+	+	–	+	–	–	+	–	+	–	–	Cured
M. S.	+	+	+	–	+	–	–	+	–	+	–	–	Cured
A. P.	+	+	+	–	+	–	–	+	–	+	–	–	Cured

Key to Table I: ART., artificial; B.B.M., boiled breast milk; BR., breast; B.T., blood transfusion; CLYSIS., hypodermoclysis; D & S, dextrose (2½%) and saline (0.4%) solution; EVAP., evaporated milk; H & D, Hartmann's dextrose solution (2½%); INT. VEN., intravenous; N.B. NUR., newborn nursery; P.P.M., powdered protein milk; R.B.M., raw breast milk; S.L.A.M., skimmed lactic acid milk; +, given; –, not given.

TABLE II

LABORATORY FINDINGS

NAME	STOOL CULT.	BLOOD CULT.	B.A.P.	URINE	R.B.C.	W.B.C.	HB %	TEMP.	PATH. IN MOTHER	RESULT
WARD 41										
M. O.	B. Pyo.	–	0	0	–	–	–	N	Scabies	Cured
A. M.*	B. Pyo.	N.G.	0	0	–	–	–	S 102	Sus. Mil. Tb.	Cured
J. H.	0	–	0	0	3.9	11.5	69	N	Kahn 1+	Cured
P. H.	–	–	–	0	–	–	–	96	Wass. 4+	Death
L. Sc.	B. Pyo.	–	–	0	5.3	13.9	98	S 104	Sus. syph.	Death
D. W.	–	–	–	–	–	–	–	S 101	Kahn 2+	Death
H. E.	B. Pyo.	–	–	Alb.	4.3	11.1	84	S 101	Wass. 1+	Death
E. P.	0	–	0	0	5.5	9.0	101	S 103	Sus. syph.	Cured
F. P.	0	–	0	0	5.2	12.3	78	N	Urt.	Cured
E. J.	B. Pyo. 0	–	0	Alb.	–	–	–	N	U. R. I. Sus. syph.	Cured
A. S.	0	–	0	0	–	–	–	S 102	Gc.	Death
WARD 51										
R. G.	B. Pyo.	N.G.	0	0	3.0	36.5	52	N	0	Cured
E. O.	0	–	0	0	3.9	12.4	63	S 104	0	Cured
C. D.*	0	S.A.	–	0	5.2	21.5	89	S 107	0	Death
B. W.	0	–	0	0	5.0	–	84	N	0	Cured
H. P.	B. Ent.	–	0	Alb.	3.0	11.4	58	S 103	0	Cured
A. K.*	B. Ent.	N.G.	0	Alb.	3.1	12.4	52	S 101	0	Cured
H. B.	0	B.S.	4+	0	–	–	–	N	0	Cured
F. B.	0	–	0	0	–	–	–	N	0	Cured
J. M.*	B. Ent.	N.G.	0	0	4.3	17.8	75	N	0	Cured
T. S.	–	–	–	0	4.3	7.4	80	S 102	0	Death
P. P.	0	–	0	0	5.7	11.8	110	N	0	Cured
C. Y.	0	–	4+	Alb.	3.5	16.2	69	S.E.	0	Cured
M. de M.*	B. Ent. B. Pyo.	A.C.	0	0	5.3	7.7	86	S.E.	0	Cured
L. Sa.*	B. Coli 0	S.A.	0	0	5.0	13.2	93	S.E.	0	Cured
M. S.	B. Pyo.	A.C.	0	0	4.2	6.9	78	S.E.	0	Cured
A. P.	0 B. Pyo.	N.G.	0	0	4.0	9.9	69	S.E.	0	Cured

*Blood agglutination negative for colon typhoid, salmonella group, and *B. pyocyaneus*.

Key to Table II: A.C., air coccus; B.A.P., blood agar plate; B. ENT., *B. enteritides*; B. PYO., *B. pyocyaneus*; B.S., *B. subtilis*; GC., gonorrhea; N.G., no growth; S., septic; S.A., *Staph. albus*; U.R.I., infection of upper respiratory; URT., urticaria; 0, negative; –, not done.

two, but a fourth resident, assigned to the prenatal clinic and not working in the first two wards, relieved him every second night. The four internes assigned to Ward 50 and Ward 51 exchanged services. The two internes on Ward 41 served their own ward only. None of the obstetric staff entered the newborn nurseries. The same attending pediatrician, resident, and interne from the pediatric department supervised all nurseries.

The nursing personnel in each of the three obstetric wards was specifically assigned to labor rooms, care of prepartum and postpartum ward patients, and the newborn infant nurseries. There was no interchange of duties and no shifting of nurses from one ward to the other. Nurses assigned to the nursery were instructed in the thorough cleansing of hands with soap and water before handling infants. The appearance of any skin lesion, abrasion, or disease in a nurse assigned to the care of the newborn infants, prohibited her from work in the unit until all symptoms had disappeared. No nurse was allowed to work in the nursery unless her nose and throat cultures were negative for hemolytic streptococci.

Infants of Wards 50 and 51 received nothing by mouth for the first eight hours and then, if the mother's condition permitted, were put to breast on a four hour schedule. Complemental feedings of raw breast milk or whole boiled or evaporated milk were offered to those who obtained an insufficient amount. On Ward 41 the feeding of the infants of mothers with normal temperature and negative serology was the same as on the other two wards. The infants of mothers with positive serology were put to the breast only if the routine x-ray examination of the long bones showed evidence of syphilis in their progeny. For the two or three days pending the x-ray report, these infants were given evaporated or whole boiled milk. Water and tea were offered between feedings to the infants on Wards 51 and 41, but not to those on Ward 50.

The complemental and supplemental feedings were prepared in the milk laboratory in the Children's Hospital, a separate building. Ward 51 received its formulas in quart bottles which were poured into individual nursing bottles in the obstetric ward kitchen. A complete sterile setup including a scrubbed nurse was part of the routine procedure in the ward. The water offered to the infants between feedings came from sterilizers in the obstetric ward and was poured into feeding bottles previously boiled in the obstetric ward kitchen.

Table III is a schematic representation of the ward routines. It will be noted that:

1. Nurseries of Wards 51, 50, and 41, were served by the same attending obstetric and pediatric staff.

2. Infants in Wards 51 and 41 only were infected; Ward 50 escaped.

3. The same residents served Wards 50 and 51 but only Ward 51 was infected.

4. Ward 41 was served by a separate set of residents, and it was infected.

5. No interchange of nursing personnel occurred in the three nurseries.

TABLE III

COMPARISON OF TECHNIQUE IN OBSTETRIC WARDS

	NORMAL OBSTETRICS	OPERATIVE AND NON-INFECTIOUS COMPLICATIONS	VENEREAL AND OTHER INFECTIONS
	WARD 51 INFECTED	WARD 50 NOT INFECTED	WARD 41 INFECTED
NURSES	INDIVIDUAL	INDIVIDUAL	INDIVIDUAL
Obstetrics			
Att. Obst.	Same	Same	Same
Resident	INTERCHANGE ⟷		Individual
Interne	INTERCHANGE ⟷		Individual
Pediatrics			
Att. Ped.	Same	Same	Same
Resident	Same	Same	Same
Interne	Same	Same	Same
Milk formulas	Prepared in Children's Hospital diet kitchen but poured in obstetric kitchen.	Prepared and poured in Children's Hospital diet kitchen.	Prepared and poured in Children's Hospital diet kitchen.
Water	Prepared and poured from sterilizer in obstetric kitchen	None used.	Prepared and poured in Children's Hospital diet kitchen.

It seems reasonable to conclude from the above analysis that the infection was not transmitted by members of the medical staff or nursing personnel.

Reports from the bacteriologic laboratory yielded the following information:*

A. *Milk*

1. *Evaporated.*—No growth was obtained from a can opened in the bacteriologic laboratory. Random samples taken in the course of preparation of formulas yielded hay bacillus, unclassified streptococci, and *Str. viridans,* each once. Five days after the outbreak, a sample of the milk and water formulas prepared by Ward 51 contained *B. pyocyaneus* and *Str. viridans.* This prompted an immediate elimination of formula preparation in the obstetric ward kitchen. Subsequent formulas were prepared in the milk laboratory of the Children's Hospital.
2. *Pasteurized.*—Cultures of the pasteurized bottled milk as delivered by the dairies yielded gram-negative rods, *Staph. albus,* and *Str. viridans* on various occasions. *B. pyocyaneus* was reported twice.

*The bacteriologic studies were done by Miss Carrie I. Woolsey, M.A., Department of Bacteriology, Cook County Hospital, without whose cooperation, this report would have been incomplete.

3. *Raw breast milk.* Cultures reported only an occasional *Staph. albus.*

B. *Sugar*

1. *Cane.*—The hay bacillus was isolated.
2. *Karo.*—*Staph. albus* and the hay bacillus were isolated.

C. *Water.* A number of samples contained *Staph. albus* and the hay bacillus. A sample from Ward 51 yielded *B. pyocyaneus* on Dec. 12, 1937.

D. *Miscellaneous*

1. *Empty capped nursing bottles from sterilizer.*—Hay bacillus and *Staph. albus.*
2. *Empty bottles from sterilizer.*—Hay bacillus.
3. *Corks for nursing bottles.*—Heavy growth of *B. pyocyaneus.*
4. *Tea.*—No growth of organisms.
5. *Dust.*—This was collected from a cupboard in the milk laboratory and yielded *B. pyocyaneus.*
6. *Simmon's plate.*—Exposed two hours in the milk laboratory, no growth.
7. *Simmon's plate.*—Exposed two hours in the kitchen of Ward 51, one colony of *B. pyocyaneus.*
8. *Blood agar plate.*—Exposed two hours in the milk laboratory with a growth of twenty-four colonies of contamination organisms, no streptococci.

E.* *Stools.* Stool cultures were done in twenty-two of the twenty-seven cases. Two or more cultures were done in most cases. *B. enteritides* was found in three, *B. pyocyaneus* in six, and in one case three cultures each yielded a different organism, namely *B. enteritides, B. pyocyaneus* and *B. coli.* In twelve cases, none of the organisms commonly associated with enteric disturbances were isolated.

F.* *Blood.* Blood cultures were done in nine cases, several being chosen from the various groups as evidenced by stool culture reports. There were five reported as "no growth," two contained an air coccus (contaminant), one had a growth of *B. subtilis* (contaminant), the remaining one yielded *Staph. albus.* Those reported as air coccus and *B. subtilis* may be regarded as negative.

Agglutination of the blood for the colon typhoid group including *B. pyocyaneus* was done in seven patients, again using cases from the various groups. All were reported as negative.

G.* *Nose and Throat Cultures.* Smears from the nose and throat of all infants in this series were plated on blood agar medium and yielded two positive cultures for the hemolytic streptococci. These were reported as four plus. Subsequent cultures became negative and both recovered.

The clinical laboratory findings were as follows:

1. *Urinalysis.**—A mild albuminuria occurred in four children, the remainder being negative.
2. *Blood Count.**—The red blood count varied from 2,740,000 to 6,170,000. The white count ranged from 5,750 to 36,500 with the latter figure occurring in an infant with suspected erythroblastosis fetalis. The hemoglobin determinations scaled from 52 per cent to 110 per cent according to the Tallqvist method.

Maternal Pathology.—All infants born on Ward 51 had mothers entirely free from recognized pathologic conditions. All infants born on Ward 41 had mothers with such pathologic conditions as positive Wassermann test, mild upper respiratory infection, gonorrhea, or scabies.

*See Table II.

TABLE IV

SUMMARY OF STOOL CULTURES

WARD	B. ENT.	B. PYO.	B. COLI.	NEG. FOR COLON TYPHOID SALMONELLA GROUP	NO CULTURE
41	0	5	0	5	2
51	4	3	1	9	1
Total	4	8	1	14	3

NOTE: MdM. } 3 stool cultures, each yielded a different organism.
A.P. }
F.P. } 2 stool cultures, each yielded different organisms.

A review of contaminating organisms of which one might be suspicious in such an epidemic revealed the following:

1. *B. pyocyaneus* was reported in the dust of the milk laboratory, supplying all wards after Dec. 12, 1937.

2. *B. pyocyaneus* was recovered from the bottle corks sent to Wards 50 and 41.

3. *B. pyocyaneus* was recovered from the water supply of Ward 51.

4. *B. pyocyaneus* was recovered from the formulas after pouring in the kitchen of Ward 51.

5. Other contaminants were found less frequently in the utensils and food used in these wards.

In spite of these findings, Ward 50, equally subjected to contamination, escaped the epidemic. One hundred and two infants in this ward were given formulas prepared in the milk laboratory with no ill effect, in contradistinction to the result in Ward 41 where eleven of twenty-nine infants fed identical formulas became ill.

These findings suggest that, despite the reported frequency of *B. pyocyaneus* as a contaminant of the food and water supply, one cannot conclude with assurance that it was the causative agent, since of two wards whose food supply was derived from the same source only one was affected.

Furthermore, it is unlikely that the infection could have been derived from the water supplied to the newborn infants since Ward 51 (infected) used water from their own sterilizer and Ward 41 (infected) received its water from the milk laboratory. It is interesting to note, however, that Ward 50 (not infected) gave no water to its infants; however, it gave complementary feedings containing water from the same milk laboratory that supplied the other two wards.

Table V is a summary of the autopsy findings in the seven who died.

The procedure employed in the control of this epidemic followed the usual routine of our newborn infant nurseries. Within twelve hours of the initial sign of illness in the first infant (Case 12), he was transferred to the Children's Division and isolated. Each succeeding case was transferred as soon as there was a suspicion of illness. Twenty-four infants became ill between Dec. 6, 1937, and Dec. 28, 1937, before it was recognized that the nurseries had to be closed in order to stamp

out the infection. During this period new cases occurred at irregular intervals. After a lapse of several days without new cases developing, a false sense of security was disrupted by the appearance of a new case. During this period the bacteriology of the food, water, and personnel was carefully investigated and resulted in the findings recorded above. It was deemed advisable because of the bacterial contamination to centralize the preparation of food in the diet kitchen of the children's division. This eliminated any source of infection which might have occurred from food and water prepared in the newborn nurseries. In spite of this change in procedure, however, the epidemic continued.

TABLE V

SUMMARY OF AUTOPSY REPORTS

MULTIPLE ABSCESSES		BRONCHO-PNEUMONIA		ENTERO-COLITIS		ENDO-CARDITIS
2		6		2		1
Bacteriology						
Heart's Blood						
Str. viridans		*B. muc. cap.*		*B. coli*		*Staph. aureus*
1		1		1		1
Gastrointestinal						
B. coli	*Staph. albus*	*Staph. aureus*	*B. muc. cap.*	*B. pyo.*	*B. prot.*	*Str. viridans*
5	3	1	2	1	2	2

On Dec. 28, 1937, both nurseries were closed, and the remaining six well infants were transferred to the Children's Division. Three of these became ill the following day, and one died (endocarditis).

The newborn ward was thoroughly cleaned and repainted and not opened for a period of two weeks.

All three wards have been in use continuously for the past fourteen months, during which time not a single case in any way resembling these has occurred.

DISCUSSION

A review of the findings at autopsy showed bronchopneumonia in six of the seven infants who died, and in only two was there anatomic evidence of enterocolitis. Multiple abscesses were found in two and endocarditis in one. Table V shows the large variability in the bacteriologic findings of the heart's blood and gastrointestinal tract at post mortem. When compared with the bacteriology reported from the stools and blood during life (Table II), it is evident that no correlation can be determined.

Rice and his associates[1] tabulated the bacteriologic reports in five epidemics from various cities. Each reported a different organism and in several epidemics, more than one organism predominated in

the stools. In the same paper they reported 505 cases of neonatal illness in sixteen epidemics in New York City and state that "numerous cultures of the stools and of the nasal and pharyngeal secretions of the sick infants gave very indefinite results. Similar cultures taken from the nurses, physicians, mothers, and other maternity and nursery service personnel also failed to reveal a causative organism."

In the New York epidemics reported by Rice and his co-workers, 234 of the 505 infants infected died, a mortality rate of 46 per cent. They showed that the fatality rate was 44 per cent in eight other epidemics occurring elsewhere. In our epidemic, death occurred in seven of twenty-seven infected infants, a fatality rate of 26 per cent.

The control of an epidemic of sepsis in a newborn ward is based upon recognition of the first case and closure of that ward until all contacts have been dismissed and the wards thoroughly cleaned before reopening.

CONCLUSION

Serious epidemics of sepsis have occurred in the newborn nurseries of many institutions. These epidemics are accompanied by a fatality rate varying between 0 and 79 per cent, the average being between 40 and 50 per cent.

The method of transmission and dissemination of infection has not been determined.

The etiology of these epidemics cannot be ascribed to a single causative agent in view of the variability of bacteriologic reports.

Epidemics have been best controlled by immediate closing and cleaning of the infected nursery and admitting no new infants until all contacts have been discharged.

In view of the post-mortem findings in this, as well as in similar epidemics elsewhere, it seems desirable that such epidemics be classified as "sepsis in the newborn infant" rather than diarrhea, until a definite etiological agent can be isolated.

The prevention of similar epidemics is based upon the most vigorous aseptic technique in the management of the newborn nursery. This technic must include exclusion of all infected individuals from the nursery and the limitation of all unnecessary handling of the newborn infants.

No specific therapy is suggested. Raw human milk feedings, whole blood, and parenteral fluids are indicated as prophylactic and supportive measures.

REFERENCE

1. Rice, J. L., Best, W. H., Frant, D., and Abramson, H.: J. A. M. A. 109: 475, 1937.

185 North Wabash

STAPHYLOCOCCUS PNEUMONIA

A Clinical, Pathologic, and Bacteriologic Study

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VERY little has been written about staphylococcus pneumonia as a disease. Chickering and Park[1] in 1919 and Reimann[2] in 1933 each reported several cases in adults. Four cases in children were reported by Smith,[3] but these terminated before the complete clinical picture had developed. MacGregor[4] described ten cases of staphylococcus pneumonia which were also fatal. No differentiation into primary and secondary pneumonia was made. Recently Anderson and Cathcart[5] reported a case which they considered primary. Other papers on the subject dealt with staphylococcus pneumonitis secondary to virus diseases, such as influenza or pertussis.

In this paper we are presenting thirty-seven cases of pneumonia in which the staphylococcus organism was the etiological agent. These cases we classify as follows:

1. Primary staphylococcus pneumonia.

2. Secondary staphylococcus pneumonia occurring in the course of a staphylococcus sepsis.

We have been especially interested in the first group. In these cases the pneumonia was the outstanding feature of the illness and dominated the clinical picture. The symptoms and the findings on physical examination closely resembled, in most instances, those found in pneumococcus pneumonia. At autopsy, however, the lungs showed infection typical of staphylococcus pathology, e.g., tissue destruction and abscess formation. Empyema was an almost constant complication.

In the second group the clinical picture was that of sepsis with a readily demonstrable extrapulmonary primary focus in the majority of cases. Most of the patients, however, did develop symptoms and signs of pneumonia at some time during the course of the sepsis with complete overshadowing of the other findings. In a few the pneumonia remained subsidiary, and the evidence of lung involvement was sparse.

In the first group there were twenty-five cases, or 68 per cent of the total. In the second group there were twelve patients, and in eight of these the pneumonia overshadowed the sepsis during some phase of the course.

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BACTERIOLOGY

The etiology in our cases was determined in one of three ways: by blood culture, culture of the empyema fluid, or by culture of the lung at autopsy. Our figures do not include cases, if they exist, which recover without having developed either bacteriemia or empyema.

The blood culture was positive in four of the twenty-five primary cases (16 per cent), but only one of these was positive during life. And in this one only the broths showed organisms, while in the three positive post-mortem cultures, there was massive invasion of broths and agar plates.

Of the patients in the secondary group, all had positive cultures during life. Ten of the twelve had massive blood stream invasions (more than ten colonies per cubic centimeter of blood); one had a moderate invasion (one to ten colonies); and one showed a slight invasion (broths positive, plates sterile).

In all instances the staphylococcus was in pure culture when isolated from the blood or empyema fluid. Post-mortem specimens showed the organism either in pure culture or predominating.

ETIOLOGY

Season.—Our cases of primary staphylococcus pneumonia followed the seasonal incidence of other types of pneumonias. They differed in this respect from other forms of staphylococcus infection. Eighty per cent of the primary cases developed during the winter and early spring, whereas only 20 per cent occurred during the summer season. On the other hand, 60 per cent of the secondary cases came during the summer months, following closely our experience in a previous study of staphylococcus bacteriemia. There was no tendency to occurrence in epidemics (Tables I and II).

TABLE I

DISTRIBUTION OF CASES BY MONTH

MONTH	PRIMARY	SECONDARY	STAPH. SEPSIS
Jan.	2	2	4
Feb.	2	0	2
March	7	0	6
April	0	1	2
May	1	3	6
June	1	0	4
July	2	0	1
Aug.	0	2	1
Sept.	0	2	4
Oct.	2	2	4
Nov.	2	1	6
Dec.	4	0	6

Sex.—The primary cases were equally distributed between males and females. Secondary pneumonia, however, was twice as frequent in males, which was also true of cases of staphylococcemia previously studied (Table III).

TABLE II

DISTRIBUTION OF CASES SEASONALLY

SEASON	PRIMARY CASES	SECONDARY CASES	STAPH. SEPSIS
J. F. M.			
O. N. D.	19	5	28
A. M. J.			
J. A. S.	5	7	18
% Cases coming in winter	80%	63%	61%
% Cases coming in summer	20%	57%	59%

TABLE III

DISTRIBUTION OF CASES ACCORDING TO SEX

	PRIMARY CASES	SECONDARY CASES	STAPH. SEPSIS
Male	12	8	30
Female	11	4	15

Age.—Seventy per cent of the primary pneumonias occurred in patients under one year of age, 21 per cent at from one to five years, and only 9 per cent were over five years of age. Of the secondary cases only 46 per cent occurred in children under one year of age, 22 per cent between one and five years, and 32 per cent were in children over five years of age. Again, the secondary cases followed an almost identical distribution as in our patients with staphylococcemia (Table IV).

TABLE IV

DISTRIBUTION OF CASES ACCORDING TO AGE

AGE (YR.)	PRIMARY CASES	SECONDARY CASES	STAPH. SEPSIS
Under 1	16	5	21
1-2	2	0	2
2-3	2	3	5
3-5	1	1	3
5-9	1	2	12
Over 9	1	1	3
% under 1	70	41	46
% over 5	9	25	32

In our cases the weight and development were good except where the pneumonia started after a long and debilitating illness (Table V). We found no other predisposing factors.

TABLE V

BIRTH WEIGHTS IN THE TWO TYPES

WEIGHT AT BIRTH	PRIMARY CASES	SECONDARY CASES
Under 6 lb.	3	0
6 lb. to 16 lb. 15 oz.	5	3
7 lb. and over	3	4
Unknown	2	5

CLINICAL PICTURE

Onset.—The onset of the primary pneumonias was fulminating, acute, or insidious. In eighteen cases the pneumonia began acutely, follow-

ing a banal upper respiratory infection of twenty-four to forty-eight hours' duration in ten, a more or less chronic upper respiratory infection in seven, and a long period of diarrhea and intestinal intoxication in one. The onset was fulminating in four cases, with a rapidly developing lung infection reaching its climax in only a few hours, without any prodromes. In two cases the onset was insidious, the pneumonia starting gradually in the course of a prolonged, mild upper respiratory infection.

There was no distinctive symptom that could be considered characteristic of the onset. In one primary case and in two secondary cases the illness was ushered in by a chill.

Fever.—Of the twenty-three cases with primary pneumonia, eight had a high sustained temperature, and two showed low sustained temperature. Ten of the twenty-three cases therefore developed a fastigial fever curve which is commonly associated with pneumonia and is usually attributed to the pneumococcic type of infection. Seven cases showed a high, irregular curve and one, a low grade irregular fever. Four had low or normal temperatures. We considered the temperature high if above 103° F., moderate if below 102° F., and sustained if the diurnal variation was less than one degree.

We believe that in any group of pneumonias caused by other organisms the same types of variation would be found. There is one difference however. A patient with pneumococcus pneumonia who shows a low, irregular temperature usually recovers quickly without displaying toxic signs. Such a temperature curve, however, in a patient with staphylococcus pneumonia often spells a long course, terminating in death.

Type of Involvement.—We are concerned with the types of consolidation rather than with a detailed account of the physical findings. Eighty per cent of the twenty-three cases of primary pneumonia presented the physical and x-ray signs typical of lobar pneumonia, and the remainder, those of bronchopneumonia. It is interesting to note that two of the twelve secondary cases also showed a lobar type of involvement. The terms lobar pneumonia and bronchopneumonia are used to describe the clinical picture and do not imply a pathologic classification. As a matter of fact, autopsy revealed scattered foci of lobular consolidation in some of the cases where the clinical and x-ray criteria indicated a lobar pneumonia.

Empyema.—Empyema occurred with such frequency in our cases that it might be considered an integral part of the disease rather than a complication. We saw it in 87 per cent of the primary cases and in 58 per cent of the secondary cases. To these may be added a patient with primary pneumonia who developed a sterile, serous effusion.

Although it is impossible to estimate accurately the time of onset of the empyema from the history, our impression is that it came early.

In fifteen cases where a rough approximation could be ventured, the average time of onset was on the sixth day after the beginning of pneumonia.

The color of the empyema pus was distinctive in some of the cases. The pus was described as pink or reddish in three cases, brown in two cases, and chocolate colored in a sixth. In the others the nature of the exudate was not characteristic, appearing either thick yellow or white or greenish, and in one case as seropurulent. In the first six cases we feel the distinctive colors indicated breaking down of tissue with bleeding into the pleural cavity.

Pyopneumothorax.—Spontaneous pneumothorax occurred only twice before chest aspiration had been attempted: in a baby girl of 7 months who died and in a girl of 30 months who recovered.

Upper Respiratory Tract Involvement.—Infection of the upper respiratory tract was a prevalent concomitant finding in the primary cases, but in the secondary cases it was only moderately frequent and never severe. Eighteen, or 80 per cent, of the primary cases had a definite acute pharyngitis. In eight of these the pharyngitis was very severe, one showing actual necrosis of the pharynx. Nine of the children (40 per cent) had acute middle ear infections. In the secondary cases four, or 33 per cent, showed a mild acute pharyngitis and only two (17 per cent) had otitis media.

Three of the primary cases presented a marked purulent nasal discharge, one accompanied by a definite sinusitis. One of the patients in the secondary group also had a sinusitis. Acute adenitis occurred in only one child in the entire series, a child with secondary pneumonia.

Distant Localizations.—Pyogenic localization outside the respiratory tract did not occur in any of the primary cases. Among the twelve secondary cases, however, five developed osteomyelitis; seven had multiple pyogenic skin infections; two developed metastatic foci in the peritoneum; and two developed abscesses in the kidneys.

Gastrointestinal Symptoms.—In the primary group abdominal distention was present in eleven cases, moderate or severe diarrhea in nine, abdominal pain in one, persistent vomiting in one, and gastrointestinal intoxication in one. The gastrointestinal symptoms in the secondary cases were also quite prominent and distressing except for the noteworthy fact that diarrhea did not occur in this group. Our impression is that gastrointestinal symptoms are much more prominent in staphylococcus pneumonia than in pneumococcus infection. In pneumococcus pneumonia distention occurs only in the very severe cases, and diarrhea only rarely.

Genitourinary Tract Involvement.—Six of the patients (25 per cent) with primary pneumonia suffered from involvement of the genitourinary tract. In four patients varying amounts of albumin ap-

peared in the urine; in one there was clinical and laboratory evidence of acute nephritis; and in the sixth ureteritis was found at autopsy. Among the secondary pneumonias there were two with perinephritis. Three of the patients in the secondary group died before renal study could be made, and they were not autopsied. Therefore, 33 per cent of the secondary cases in whom the urinary status was known showed some type of involvement.

Circulatory System.—Cyanosis was a prominent symptom in all groups. It appeared at one time or another in eighteen of the primary cases and seven of the secondary cases. In one primary case and in one secondary case transient murmurs at the precordium were elicited.

Nervous System.—Symptoms of nervous system involvement occurred infrequently (about 12 per cent of all cases) and were not distinctive for either group. Delirium, drowsiness, and meningismus were the usual manifestations, when present. On autopsy there were two instances of intense cerebral congestion (primary cases), one cerebral hemorrhage and one case of toxic encephalitis (secondary cases).

Hematopoietic System.—No special hematologic studies were made. We present the results gleaned from routine studies performed on patients with primary staphylococcus pneumonia. The total white blood cell count varied considerably. In two patients there was a leucopenia of 3,000 and 4,000 cells. Three gave a normal count, seven showed a moderate leucocytosis up to 20,000 white cells; in three the white cell count was above 20,000, and in seven it was above 30,000.

The relative percentage of the polymorphonuclear cells was high in only a few cases: four of the cases gave a percentage of 60; five were under 60 per cent; and thirteen were above 70 per cent. There was, however, a high proportion of immature cells in most smears. This proved to be of importance in the prognosis.

Hemoglobin studies could not be made accurately due to the fact that most of the patients received one or more transfusions during the course of their illness. A Sahli hemoglobin determination was made on each admission and was usually low: only eleven of the twenty-three primary cases showed a reading above 70 per cent.

Duration.—In the primary cases the average duration of the illness in those who recovered was twenty-nine days, and ten days in patients who died. We found these figures similar to those in our series of cases of staphylococcus sepsis.

Prognosis.—Seventy-three per cent of our patients with staphylococcus pneumonia died. The mortality was 65 per cent in the primary group and 83 per cent in the secondary group. This is a high mortality especially when compared with our figures of 56.6 per cent mortality in cases of staphylococcus sepsis.

Infants under 1 year of age suffered the highest mortality and accounted for most of the deaths. Seventy per cent of the patients who

developed primary pneumonia under one year of age died. With secondary pneumonia the mortality was 100 per cent during the first year of life.

A high, sustained fever curve may be considered indicative of a poor prognosis, but an irregular curve, whether at a high or a low level, was usually associated with a favorable outcome. Of the fifteen patients with primary pneumonia who died, nine had a high sustained (fastigial) temperature, two had an irregular temperature with high peaks, and one had a moderate irregular curve. On the other hand, of the eight patients with primary cases who recovered, only one had sustained temperature elevation.

Of the eight patients with primary pneumonia who recovered, seven had signs of a lobar consolidation, and only one had a bronchopneumonic type of involvement. On the other hand all the patients who suffered from lobular types of infection died.

The blood count was an important guide in prognosis. No patient with a low or normal white cell count recovered. The hemoglobin content seemed to have no bearing on the prognosis.

From our analysis we may conclude that staphylococcus pneumonia is a disease in which the mortality is high and in which the patients who recover are sick for a long time. The factors that indicate an unfavorable outlook are infancy (onset under one year of age), an antecedent debilitating disease, bronchopneumonic type of involvement, and leucopenia.

PATHOLOGY

Nine of the primary and nine of the secondary cases came to necropsy. The study of the post-mortem picture corroborated the classification into primary and secondary pneumonia. In the primary cases the pathology was confined essentially to the lungs. In the secondary cases there were in addition suppurative foci in other parts of the body. The structures involved, in their order of frequency, were the bones, kidneys, myocardium, adrenals, pancreas, and the voluntary striated muscles. In the primary cases the findings pointed to a bronchogenic origin of the infection. In the secondary cases no matter how extensive the destruction of the lung parenchyma was, it was not difficult to find evidence that this was secondary in nature, as indicated by the presence of infected thrombi in the blood vessels, surrounded by areas of infarction and abscess formation.

The picture in most of the primary cases was quite typical. On opening the pleural cavity the lungs were usually found bathed in purulent fluid of a creamy, greenish color or a reddish or chocolate color. In seven instances there were adhesions between the parietal and visceral pleura. The pleura was thickened, frequently shaggy, and of a gray color. The surface of the lung, especially over a lower

lobe, was studded with small mulberry-like yellowish nodules, "carbuncles," from which creamy pus could be evacuated. The cut surfaces revealed many more of these small abscesses (Fig. 1). In two cases there were a few small foci in the opposite lung.

Fig. 1.—Cut surface of lung.

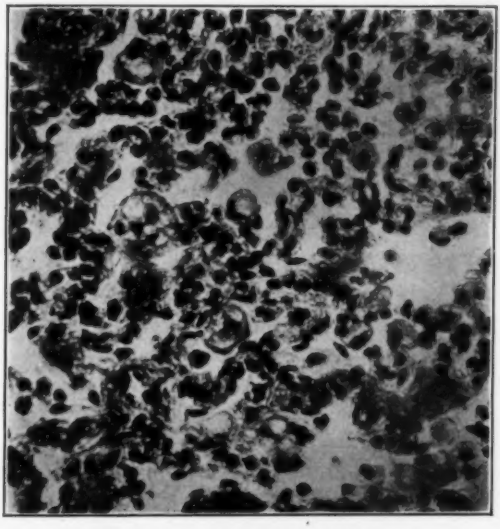

Fig. 2.—"Lipoid" cells (×800).

Microscopic Examination.—There were numerous fairly well circumscribed areas in which the lung architecture was absent, and the centers were made of polymorphonuclear leucocytes. From a little to a moderate amount of fibrin was present in the surrounding zone of parenchyma. Here, the alveoli were filled with polymorphonuclear

leucocytes, few mononuclear cells, and red blood cells. In one instance, this area was markedly emphysematous, and in another the alveolar walls were collapsed. In another case the alveoli contained large pale cells filled with vacuoles, which stained with sudan III (Fig. 2).

The bronchi and bronchioles were filled with polymorphonuclear leucocytes. In some places the bronchial mucosa was absent, the walls infiltrated with leucocytes and mononuclear cells, the capillaries in the walls numerous and distended with red blood cells. Frequently these terminal bronchi communicated with an adjoining abscess.

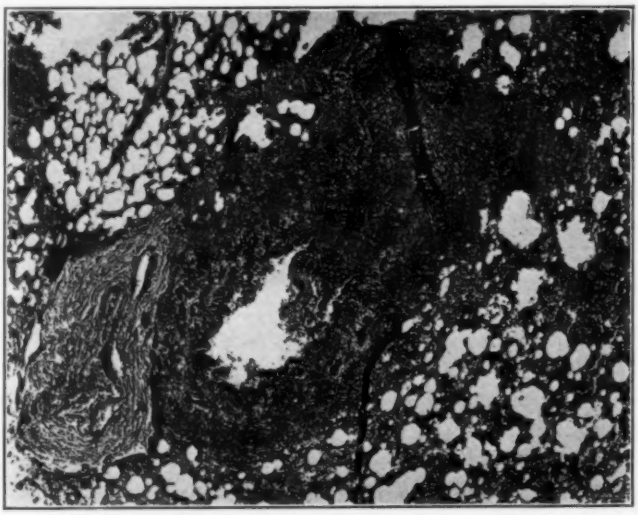

Fig. 3.—Purulent bronchitis (×67).

A somewhat different picture presented itself in one of this group. The pleural cavity contained considerable cloudy hemorrhagic fluid. The pleura over the left lower lobe was thickened and shaggy. The left lower lobe was almost entirely solid. There were firm nodular areas in the remaining lobes. The cut surface was dark red, moist, and friable and, when scraped with a knife, presented minute pockets of pus. The mucosa of the pharynx, trachea, and bronchi was a red gray, and the latter contained sanguinopurulent material. Microscopic examination of the left lower lobe revealed extensive hemolysis of red blood cells with only ghosts of cells remaining and numerous polymorphonuclear leucocytes dispersed among them. In some of these areas the lung architecture was entirely absent, and in the center of these, clumps of bacteria were present.

Two of the cases in which the pleural cavity contained no free fluid presented the following picture: In the first, there were few thin

fibrinous adhesions between the lung and pleura. The posterior portion of the lower lobes presented dark red, moist areas, and the cut surfaces presented small gray patches of consolidation. Microscopic examination showed that these small patches of consolidation were located about the terminal bronchi and bronchioles (Fig. 3).

The lumina of these and adjoining alveoli were completely filled with numerous polymorphonuclear leucocytes and few mononuclear cells. The alveolar septa were broadened, and their capillaries were distended. The epithelium of some of the bronchi was absent. The capillaries in their walls were distended, and the walls themselves contained polymorphonuclear leucocytes and small and large mononuclear cells.

Fig. 4.—Abscess with clumps of bacteria (×65).

In the other case the epiglottis, larynx, trachea, and bronchi were covered with a necrotic fibrinopurulent exudate. The mucosa of the larynx was ulcerated. The tracheal mucosa was necrotic, and this process extended into the mucous glands. The lungs were voluminous, and a fibrinous exudate was present over the posterior and diaphragmatic surfaces of the lower lobes. The lower lobes were firm and nodular. The cut surfaces presented brownish-red consolidated areas and minute abscesses.

Microscopic Examination.—There were numerous hemorrhagic areas, in which the alveolar walls were barely discernible and in which the red cells blended into a homogenous mass. Toward the center of the hemorrhagic zone, there was another zone made up of large mononuclear cells with few leucocytes. The alveolar walls were barely

recognizable. In the center there were clumps of bacteria surrounded by cells with pyknotic nuclei (Fig. 4). An adjoining artery showed numerous cells loaded with bacteria.

The remaining organs in this group presented nothing unusual, with the exception of the one infant, who also showed an interstitial hepatitis and fibrosis of the pancreas. Sections of these organs were carefully searched for spirochetes, but none were found.

Secondary Group.—In this group an entirely different picture presented itself at necropsy. In nearly all of them an osteomyelitis was present. Abscesses were found in many of the other organs as well as the lungs. They were present in the kidneys, myocardium, adrenals, pancreas, and voluntary striated muscles. In a few instances a purulent pericarditis was also present. In the lungs and kidneys the conglomerate miliary abscesses when seen on the surface of the organs appeared as "carbuncles."

DISCUSSION

The separation of our cases into two groups was based on clinical, bacteriologic, and pathologic differences. In the primary cases the history was chiefly that of an upper respiratory tract infection, with subsequent extension of the inflammatory process to the lungs. In the secondary cases the history was that of a sepsis with the development of the pneumonia as an additional and often terminal incident. In the primary cases the physical findings were limited to the respiratory tract. In the secondary cases the clinical picture was dominated by the symptoms referable to primary and suppurative foci other than the lungs. In the patients with primary pneumonia blood cultures were sterile, or at most only evanescent bacterial invasions were demonstrable. In the secondary cases the blood stream invasion was heavy and persistent. The primary cases on autopsy showed pathology limited almost entirely to the lungs. Microscopic examination showed alveolar damage with no evidence of embolic phenomena in the blood vessels of the lung. In the secondary cases there was involvement not only in the lung, but throughout the body, and the pulmonary blood vessels showed widespread embolization. We have no evidence as to the pathogenesis of the disease in all our cases, but a study of the pathology seems to indicate that in the primary cases the portal of entry was bronchogenic. In most of the cases the lesions were almost entirely arranged about the terminal bronchi and bronchioles. In one instance a necrotic process extended from the epiglottis directly into the parenchyma of the lung. In another case, as illustrated in Fig. 2, a lipoid type of reaction was present, indicating aspiration of some foreign material.

We were interested in the significance of the bacteriemia in some of the primary cases. We feel that these small invasions of short

duration have the same relationship to primary staphylococcus pneumonia as the transitory early pneumococcemia has to pneumococcus pneumonia. It does not necessarily mean that the pneumonia was secondary to a sepsis.

The role of the staphylococcus organism in the primary cases calls for some comment. In the great influenza epidemics the staphylococcus was often found in the lungs at autopsy and was considered a secondary invader. Although we consider the staphylococcus as the essential etiological agent in our primary cases, the possibility of a virus having been the predisposing cause must also be considered. Many of our cases did resemble patients with acute influenza.

There were a few interesting facts brought out regarding staphylococcus infection. Secondary staphylococcus pneumonia followed the usual tendency of staphylococcus infection. Secondary staphylococcus pneumonia followed the usual tendency of staphylococcus infection to occur in the summer time, but primary staphylococcus invasion of the lung was much more frequent during the winter and early spring months. So far as age was concerned, the primary cases occurred chiefly in patients under 1 year of age, whereas other types of staphylococcus infection are more prone to affect older children. Secondary staphylococcus pneumonia followed the same tendency as other forms of staphylococcus infections to predominate in the male, but the primary cases were equally distributed between both sexes. It was interesting to note that the mortality in staphylococcus sepsis with lung involvement is much higher than in staphylococcemia per se. The mortality of primary staphylococcus pneumonia on the other hand is only moderately higher than the general series of cases of staphylococcus sepsis.

The resemblances to, and the differences from, pneumococcus pneumonia were of great interest. The pathology of staphylococcus pneumonia resembles in many ways the pathology of staphylococcus infection elsewhere in the body. The pathogenesis is similar to that of pneumococcus pneumonia. The clinical picture in some particulars closely resembles, and in other ways is in distinct contrast to, the pneumococcus pneumonias.

The points of resemblance between primary staphylococcus pneumonia and primary pneumococcus pneumonia are as follows:

1. There is the same incidence of positive blood cultures.
2. There is the same distribution of cases in the winter and early spring months.
3. There is the same relationship of upper respiratory infection and lung infection.
4. Many cases have the same type of fastigial temperature commonly associated with pneumococcus infection.
5. Many cases have the same type of acute onset.

6. Most of the cases had the physical findings associated with a lobar distribution of the infection.

7. Most of the patients had definite, and often severe, associated upper respiratory infection.

8. There were no distant pyogenic localizations.

9. The white counts varied from low to very high; the low counts were associated with a fatal prognosis.

The points of difference between primary staphylococcus pneumonia and primary pneumococcus pneumonia were:

1. The staphylococcus cases occurred predominantly below the age of one year.

2. The onset and course in staphylococcus cases were more often fulminating in a previously healthy child.

3. The onset in the course of a chronic illness could be so insidious that a diagnosis was made only after, or a short time before, death or during the last days of life.

4. Empyema occurred in more than three-fourths of the staphylococcus cases.

5. Pyopneumothorax occurred in two cases.

6. The empyema fluid in about 20 per cent of the cases indicated there were destruction of tissue and bleeding into the pleural cavity.

7. In the staphylococcus cases there is a greater tendency for the occurrence of diarrhea and distention.

8. There is also a greater tendency toward the appearance of renal involvement.

9. The mortality in the staphylococcus pneumonia was 65 per cent: overwhelmingly greater than in the pneumococcus cases observed by us or reported by others.

SUMMARY

Thirty-seven cases of staphylococcus pneumonia are classified and the clinical features described. The pathology and bacteriology are described in different types of cases, and the pathogenesis is discussed. A summary of the differences from, and similarities to, pneumococcus pneumonia is given.

REFERENCES

1. Chickering, H. T., and Park, J. H.: J. A. M. A. **72**: 617, 1919.
2. Reimann, H. A.: J. A. M. A. **101**: 514, 1933.
3. Smith, C. M.: Lancet **1**: 1204, 1935.
4. MacGregor, A.: Arch. Dis. Child. **11**: 195, 1936.
5. Anderson, and Cathcart: Am. J. Dis. Child. **49**: 1276, 1935.

IRRADIATED EVAPORATED MILK AS A FOOD FOR INFANTS

A Study of Growth, Elimination, Protection From Rickets, and Morbidity in Upper Respiratory Infections in Comparative Groups Fed on Irradiated and Nonirradiated Evaporated Milk

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IRRADIATED evaporated milk has been used extensively in the feeding of babies. It was the impression of one of us (H. N. S.) that babies fed this food were more likely to develop diarrhea than were infants on nonirradiated evaporated milk. While nothing on the subject has been published, so far as we know, there has been a rather widespread impression that this is true. At least, we have heard it from several different parts of the country. It seemed only fair, therefore, to make a comparative study of the two foods, namely, nonirradiated and irradiated evaporated milk, as thoroughly controlled as possible to determine whether this impression was justified.

In the course of this study in order to make a proper comparison, it was felt that we should also have a record of disease conditions, especially upper respiratory infections, and incidentally information on whether or not these children developed subclinical or clinical rickets. The infants studied came to the Welfare Station of the Central Free Dispensary, Chicago, which is a teaching center for the Rush Medical College. They live in the immediate neighborhood, which is a slum area. The babies selected were in good physical condition, and when the study started, all of them were under three months of age, most of them about six weeks old. They were followed until they were one year old; no baby is included in the study who was not under observation for at least three months. The study continued for two years so that the seasonal variation is not a matter of concern. We began in November, 1936, and continued until November, 1938, and a total of two hundred infants was observed.

The infants, as they were registered in the clinic, were placed alternately on feedings of irradiated and nonirradiated evaporated milk. The milk was bought in the open market and the labels removed. Milk was supplied weekly to the families in the quantity needed. Each child was fed 1 oz. of evaporated milk per pound body weight and 5 per cent carbohydrate in the form of cane sugar. The

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group fed nonirradiated evaporated milk was given in addition viosterol 100-D; in the beginning 10 drops a day and later 20 drops a day since in one instance 10 drops unfortunately failed to prevent the appearance of rickets in the roentgenograms. Cereal was added at four months, vegetables at five months, egg at six months, and a second cereal at eight months to the diets of all babies.

In the early part of the study, the nurse made a daily visit to each family to obtain the stool record. As the number of infants in the study increased, it became necessary to reduce the number of visits to one a week. However, between these visits the child was brought to the Station where a stool history was again taken. Thus a stool history was obtained every three or four days. In every instance where an increased number of stools was recorded, the nurse visited that child in the home daily and checked on the number of stools until the condition had improved. The same was true when respiratory infections were reported. The children were examined every two weeks by the physician in the Infant Welfare Clinic, where, besides the usual physical examination, the children were checked for signs of rickets. Roentgenograms of the long bones were taken at three-month intervals.

RESULTS

Of 103 infants who were given irradiated evaporated milk, 68 per cent were studied for one year. Of the 89 infants on nonirradiated evaporated milk, 70 per cent were studied for one year. The average number of stools per day for infants on irradiated evaporated milk was 2.0 and for those on nonirradiated evaporated milk 2.3. There were 144 upper respiratory infections during the entire period, or an average of 1.4 per infant in the group given irradiated evaporated milk, and 101, or an average of 1.1 per infant, in the group given nonirradiated evaporated milk. In the group given irradiated milk 36 of the infants had more than one cold and in the nonirradiated group, 24.

Inasmuch as two stools per day seemed to be about the average for both groups, it was decided to consider separately all infants having more than three stools per day for at least forty-eight hours. These cases were divided into two groups, (1) those in which the diarrhea was accompanied by respiratory infections and (2) those in which there was no such etiological factor evident.

In the group given irradiated evaporated milk there were 109 instances of babies having more than three stools per day for more than forty-eight hours. This is an average of 1.06 attacks per baby for the study period. Of these 109 instances, 28, or 25.7 per cent, were accompanied by upper respiratory infections, and 81, or 74.3 per cent, were not. In the group given nonirradiated evaporated milk there were 84 cases of babies having more than three stools per

day for more than forty-eight hours. This is an average of 0.94 attacks per day for the study period. Of these 84 instances, 23, or 27.4 per cent, were accompanied by upper respiratory infections and 61, or 72.6 per cent, were not (Table I).

TABLE I

TYPE OF FEEDING	NO. OF INFANTS STUDIED	AVERAGE NO. OF STOOLS PER DAY	NO. OF ATTACKS OF MORE THAN 3 STOOLS PER DAY FOR MORE THAN 48 HR.	AVERAGE NO. OF ATTACKS PER INFANT DURING STUDY PERIOD	ATTACKS WITH UPPER RESPIRATORY INFECTIONS		ATTACKS WITHOUT UPPER RESPIRATORY INFECTION	
					NO.	PER CENT	NO.	PER CENT
Irradiated evaporated milk	103	2.0	109	1.06	28	25.7	81	74.3
Non-irradiated evaporated milk	89	2.3	84	0.94	23	27.4	61	72.6

The incidence of these cases of increased stools was higher during the early months. This is true for both types of feeding. At the earliest age (1 month) the incidence of increased stools was greater in the nonirradiated group. Throughout the balance of the study, excepting in the sixth and ninth months, this ratio changed, and the irradiated group showed a somewhat higher incidence of increased stools. There were two infants in the irradiated group who were hospitalized for diarrhea which cleared up, however, without changing the type of feeding.

The only deaths in the group occurred in the nonirradiated milk group: three infants died, one each, of congenital syphilis, pneumonia, and leucemia. There were four cases of eczema in each group. The average gain in weight was 1.3 pounds per month in each group. In the group on irradiated milk no signs of rickets either clinical or roentgenographic were found, while four infants in the group given nonirradiated evaporated milk and viosterol showed slight signs of clinical rickets. This was confirmed in only one instance by x-ray.

DISCUSSION

These groups of infants in which alternate babies were given irradiated evaporated milk and nonirradiated evaporated milk, respectively, were followed for a period of two years. The seasons and age groups were similar, and the average number of stools per day was practically the same for both groups. In fact, those given the nonirradiated evaporated milk had a slightly higher average number of stools than those given the irradiated evaporated milk. We can assume, there-

fore, that in a carefully controlled study there is no greater frequency of stools in infants fed the one type of milk than the other.

It was true in this study that certain babies given nonirradiated evaporated milk showed a tendency during the early weeks toward an increased number of stools, while in later months the opposite was true. However, it must be understood that in no sense of the word is this increased number of stools to be considered pathologic and in ordinary practice the increase would probably be overlooked. It is true that two infants in this group were hospitalized for diarrhea, but two infants in a series of 192 babies is too small a number to be considered as any indication. Also it must be remembered that we were dealing with an economic group in which it is very hard to maintain a good sterile technique. In both groups there was a tendency for an increased number of stools in the younger infants.

The incidence of upper respiratory infection was high in both groups. It was higher in the group given irradiated evaporated milk than those given nonirradiated evaporated milk. For this we have no explanation. The nonirradiated evaporated milk group was given viosterol or vitamin D only, so that there was no advantage in the amount of vitamin A to either group. It had to be obtained from the milk in both cases.

We were particularly impressed with the absence of rickets in the group of infants given irradiated evaporated milk. It is often stated that certain babies cannot obtain enough protection from rickets on irradiated evaporated milk. Certainly when 103 infants raised under the social conditions of this district show no clinical or roentgenologic signs of rickets, it speaks well for the antirachitic qualities of irradiated evaporated milk. As stated at first, the babies given nonirradiated evaporated milk were given 10 drops of viosterol 100-D a day. In the very first roentgenograms taken one of these infants showed signs of rickets. The amount of viosterol was then increased to 20 drops a day. This resulted in control of this infant, and none in the future showed any signs of rickets by roentgenogram.

The frequency of infantile eczema was practically the same in each group as one would expect. Incidentally these eczemas were not as severe as are found in some breast-fed infants.

The gain in weight was exactly the same for each group.

SUMMARY

In a study carried on for two years with a group of infants given irradiated evaporated milk and nonirradiated evaporated milk and viosterol, the following facts were observed:

1. The average number of stools was practically the same for each group (2.0 per day for the irradiated milk group and 2.3 per day for the nonirradiated milk group).

2. In certain of the babies in both groups, there was a tendency occasionally to have more than three stools per day. This tendency occurred oftener in younger infants. It was slightly more marked during the first weeks in the nonirradiated milk group and during the later months in the irradiated group.

3. The average gain per month was the same in both groups (1.3 pounds per month).

4. None of the infants in the group given irradiated evaporated milk showed any signs of rickets either clinically or roentgenologically. Four infants in the group given nonirradiated evaporated milk and viosterol showed slight signs of clinical rickets, but of these only one showed signs of rickets by roentgenogram.

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PREVENTION OF PURULENT OTITIS MEDIA IN INFANTS

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OTITIS media is more frequent in infancy than during any other period of life. It is usually secondary to nasopharyngeal infections, particularly rhinitis; pneumonia; the exanthemas, particularly scarlet fever and measles; and acute intestinal intoxication. Marriott[1] and others[2] believe it to be causally related to intestinal disturbances; and this viewpoint is probably responsible for many premature and unwarranted paracenteses.

The pediatrician and general practitioner, rather than the otologist, are generally the first to encounter this disease, and they are usually called upon to advise as to its proper management. They must, therefore, be well acquainted with the pathology, symptoms, and physical signs of otitic infections.

The middle ear and the mastoid sinus are extensions from the nasopharynx and communicate with it through the eustachian tube, a short canal which runs laterally, slightly upward, and backward from the nasopharynx to the anterior wall of the tympanum. In the infant the canal is about 15 mm. long, is straight and nearly horizontal, and has a lumen of adult proportions. Lymphoid tissue is found at the pharyngeal orifice in close proximity to the other lymphoid structures of the pharynx. A short, wide direct route is thus formed for the extension of infection from the nasopharynx to the middle ear.

Clinical observation over a period of years has led us to believe that myringotomy is practiced too freely in infants and that resolution of the exudate in the middle ear often follows conservative treatment. For the past five years (1934-1938) rigid criteria for incising the membrane have been set up on the Children's Medical Service at Bellevue Hospital, and myringotomy is performed only with the approval of an attending physician. The indications for myringotomy are complete obliteration of the landmarks, especially the short process, a bulging gray drum, together with fever, restlessness, and disturbed sleep. When the pain seems intense, together with great restlessness and loss of sleep, the above criteria may be modified.

Frequent examinations by the house staff are discouraged since the proximity necessary for the otoscopic examination exposes the infant to the expired air of the examiner thereby increasing the hazard of respiratory infection in the child. Furthermore, manipulation in the canal, by traumatizing an already inflamed drum, may aggravate the

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Read at the annual meeting of the Medical Society of the State of New York, May, 1938.

condition further. To minimize the danger of infecting the infant by the physician, all ear examinations are made with the infant lying on the abdomen, the head being turned away from the examiner. Physicians with respiratory infections are warned against making otoscopic examinations.

These observations were made on a ward for acute conditions for infants under 2 years, and the conclusions are therefore limited to this age group. A three-year period, 1931-1933, was used as a control. The term purulent otitis media as here used means a purulent discharge from the ear.

Table I is a summary and includes data on which most of the charts and tables are based.

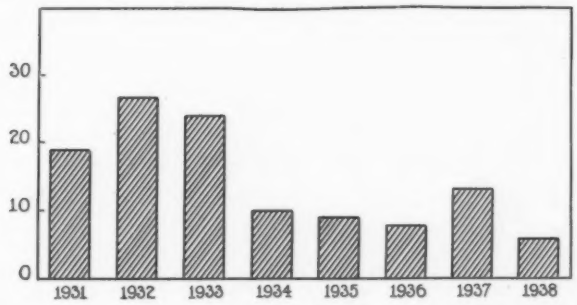

Chart 1.—The incidence of purulent otitis media in percentage of admissions.

Chart 1 illustrates the incidence of purulent otitis media, in percentage of all ward admissions, for the years 1931-1938. The dramatic drop after 1933 is evident. During the control period (1931-1933) 23.3 per cent of all patients admitted had purulent otitis whereas only 8.9 per cent suffered from this condition during 1934-1938, a reduction of 62 per cent.

TABLE I

THE INCIDENCE OF PURULENT OTITIS MEDIA FOLLOWING MYRINGOTOMY AND SPONTANEOUS RUPTURE AND THE INCIDENCE OF BILATERAL AND UNILATERAL OTITIS MEDIA

YEAR	NUMBER OF WARD ADMISSIONS	NUMBER OF INFANTS WITH PURULENT OTITIS MEDIA			NUMBER OF INFANTS WITH BILATERAL PURULENT OTITIS MEDIA	NUMBER OF INFANTS WITH UNILATERAL PURULENT OTITIS MEDIA
		TOTAL	AFTER MYRINGOTOMY	SPONTANEOUS RUPTURE		
1931	996	189	127	62	121	68
1932	842	227	146	81	154	73
1933	766	190	132	58	116	74
1931-1933	*2604*	*606*	*405*	*201*	*391*	*215*
1934	725	72	28	44	35	37
1935	752	62	29	33	25	37
1936	780	55	27	28	30	25
1937	693	90	53	37	48	42
1938	644	42	21	21	13	29
1934-1938	*3594*	*321*	*158*	*163*	*151*	*170*

Chart 2 illustrates the incidence of bilateral and unilateral purulent otitis media. The more striking reduction in the occurrence of bilateral otitis is apparent. During the years 1931-1933 there were 1.8 times as many infants with bilateral purulent otitis as unilateral, whereas during 1934-1938 the number of unilateral cases exceeded the bilateral. This

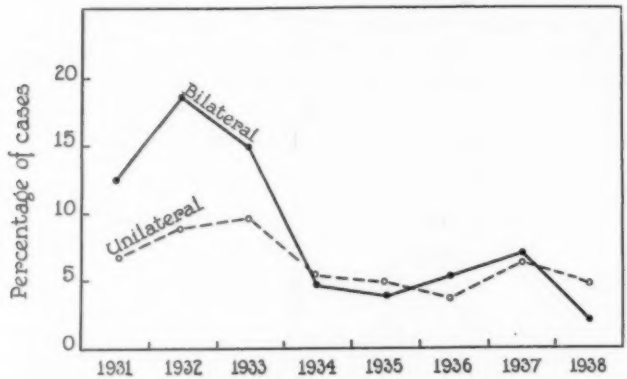

Chart 2.—The incidence of bilateral and unilateral purulent otitis media.

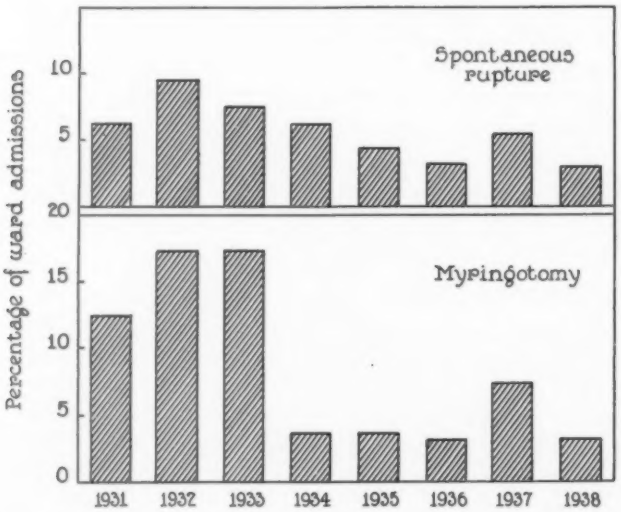

Chart 3.—The incidence of purulent otitis media after myringotomy and spontaneous rupture.

means that, during the supervised period, there was not only a reduction in the number of infants with purulent otitis media, but that, in contrast to the control period, bilateral otitis media was no more frequent than unilateral.

In Chart 3 the incidence of purulent otitis media after myringotomy and after spontaneous rupture is compared. The reduction in purulent otitis media following myringotomy is striking (from 15.6 per cent of all ward admissions, 1931-1933, to 4.4 per cent, 1934-1938). There was also a fall in the cases following spontaneous rupture (from 7.7 per cent of all ward admissions, 1931-1933, to 4.5 per cent, 1934-1938). With conservative treatment one might have expected an increase rather than a decrease in this group. That this did not occur is probably dependent on a number of factors. Frequent examinations, particularly by the inexperienced, may lead to trauma of the already inflamed drum, thereby aggravating the otitic infection. Furthermore there is danger that

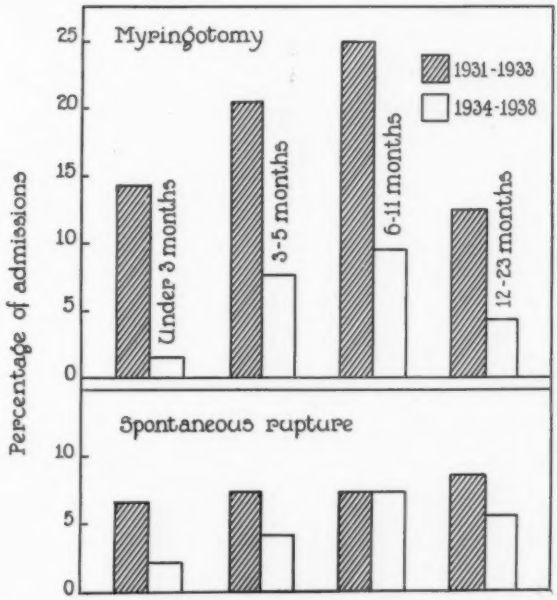

Chart 4.—The incidence of purulent otitis media by certain subdivisions of age under 2 years.

the infant's nasopharynx may be infected by the examiner; and this is naturally more likely to occur the more frequent are the examinations. Since otitis media is so often a complication of nasopharyngitis, this would lead to an increase in the incidence of otitis media. It has also been our impression that a diagnosis of spontaneous rupture is often erroneously made where a little moisture is seen on the drum.

In Chart 4 the annual incidence of otitis media, by certain subdivisions of age under 2 years, is compared for the two periods (1931-1933 and 1934-1938). The data for this chart were calculated in percentages of infants admitted in the various age groups. There has been

a reduction in the occurrence of purulent otitis media in all age subdivisions. The fall was most striking in the age group under 3 months where purulent otitis media after myringotomy dropped from 14.4 to 1.8 per cent, and after spontaneous rupture from 6.7 to 1.8 per cent. Purulent otitis media is unusual in young infants, the total incidence under 3 months during the supervised period being only 3.5 per cent.

Tables II and III, respectively, show the incidence of purulent otitis media in pneumonia (all forms) and in diarrheal diseases. In both disease groups the incidence of purulent otitis media has been reduced to approximately one-third between 1931 and 1938. The data on diarrheal diseases are of particular interest since the belief still persists that many instances of intestinal intoxication are specifically related to middle ear infections.

TABLE II
THE INCIDENCE OF PURULENT OTITIS MEDIA IN INFANTS WITH PNEUMONIA (ALL FORMS)

YEAR	NUMBER OF INFANTS WITH PNEUMONIA	NUMBER OF INFANTS WITH PURULENT OTITIS MEDIA	PERCENTAGE OF INFANTS WITH PURULENT OTITIS MEDIA
1931	111	39	35
1932	128	58	45
1933	141	36	26
1931-1933	*380*	*133*	*35.0*
1934	111	10	9
1935	92	9	10
1936	97	7	7
1937	73	22	30
1938	70	11	16
1934-1938	*443*	*59*	*13.3*

TABLE III
THE INCIDENCE OF PURULENT OTITIS MEDIA IN INFANTS WITH DIARRHEA

YEAR	NUMBER OF INFANTS WITH DIARRHEA	NUMBER OF INFANTS WITH PURULENT OTITIS MEDIA	PERCENTAGE OF INFANTS WITH PURULENT OTITIS MEDIA
1931	94	22	23
1932	78	36	46
1933	96	22	23
1931-1933	*268*	*80*	*26.7*
1934	60	8	13
1935	64	4	6
1936	75	2	3
1937	63	7	11
1938	81	5	6
1934-1938	*343*	*26*	*7.6*

In Table IV is shown the number of infants operated on for mastoiditis. The percentage of operative cases fell from 1.38 per cent of all admissions during 1931-1933 to 0.56 per cent during 1934-1938, a drop to less than half. Of the infants with purulent otitis media, the percentage operated on for mastoiditis during the two periods remained about the same (1931-1933, 5.9 per cent; 1934-1938, 6.2 per cent).

TABLE IV

THE INCIDENCE OF MASTOID DISEASE

YEAR	NUMBER OF ADMISSIONS	NUMBER OF INFANTS OPERATED FOR MASTOID DISEASE	PERCENTAGE OF ADMISSIONS OPERATED FOR MASTOID DISEASE
1931	996	9	0.9
1932	842	10	1.3
1933	766	17	2.2
1931-1933	*2604*	*36*	*1.38*
1934	725	3	0.4
1935	752	6	0.8
1936	780	4	0.5
1937	693	5	0.7
1938	644	2	0.3
1934-1938	*3594*	*20*	*0.56*

DISCUSSION

These observations demonstrate that incising an inflamed drum often leads to a purulent discharge in an ear in which, if there were no operative interference, the infection would spontaneously subside. Furthermore, the results strongly indicate that frequent examinations of the ear, by traumatizing the drum and the canal and by exposing the nasopharynx of the infant to the expired air of the examiner, favor the development of purulent otitis media. It is of interest in this connection to quote the opinion of a prominent otologist[3]: "As a result of long observations, it has become evident that to incise the drum too early in the course of the development of an acute suppuration of the middle ear is to add a factor toward the promotion, rather than toward the retardation of the middle ear infection." A similarly conservative view is voiced by Brennemann,[4] who states that "the practical measure of bulging is the short process. So long as it is in evidence even as a tiny spot, there is rarely an indication for immediate paracentesis. When it is gone, the indication commonly exists but not always. An acutely bulging drum may subside spontaneously."

In many pediatric hospitals otitis media is treated casually and its management left to the house officers without adequate supervision by the visiting staff. This attitude is fraught with danger since it exposes children, already ill, to the danger and inconvenience of unnecessary paracenteses and purulent otitic discharges. Though mastoid disease is uncommon in infants, it does occur and is to be avoided if possible.

The data in the tables and charts show how, with careful supervision, strict adherence to a standardized set of indications and avoidance of too frequent examinations, the incidence of purulent otitis media may be reduced and the danger of mastoid disease lessened.

The results of this study lend no support to the view that delay in incising an ear drum is harmful to the child. Where doubt exists,

we believe that it is preferable to wait. In acute intestinal intoxication, where a specific relationship to otitis media purulenta acuta has been hypothecated, the incidence of aural discharge has been reduced to one-third, with a fall rather than a rise in case fatality from this serious disease.

SUMMARY AND CONCLUSIONS

During 1934-1938 the management of otitis media on the Children's Medical Service, Bellevue Hospital, has been carefully supervised and a strict set of indications for myringotomy set up. The incidence of purulent otitis media during this period was compared with that during a control period (1931-1933).

The incidence of purulent otitis media was reduced from 23.3 per cent of all admissions in 1931-1933 to 8.9 per cent of all admissions in 1934-1938.

Whereas, during the control period (1931-1933) 1.8 times as many infants had bilateral purulent otitis media as unilateral, during the supervised period (1934-1938) the number of unilateral cases actually exceeded the bilateral.

The incidence of purulent otitis media among the infants with diarrheal diseases and with pneumonia was reduced to less than one-third during the supervised period.

Operations for mastoid disease were reduced from 1.38 per cent of all ward admissions during the control period to 0.56 per cent during the supervised period.

REFERENCES

1. Marriott, W. M.: Ann. Otol. Rhin. & Laryng. **36**: 686, 1927.
2. a. Holselaw, F. M., Boehm, C. A., and Bierman, J. M.: Am. J. Dis. Child. **39**: 747, 1930.
   b. Horner, C. E.: California & West. Med. **34**: 156, 1931.
   c. Rumpf, C. W.: Minnesota Med. **12**: 694, 1929.
3. Kopetzky, S. J.: Otological Surgery, New York, 1929, p. 60.
4. Brennemann, J.: J. A. M. A. **97**: 449, 1931.

REPEATED GLUCOSE TOLERANCE TESTS IN CHILDREN

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THIS study comprises repeated glucose tolerance tests on children in the first and the second decades. My object was mainly to see if the curve obtained at first examination remains unchanged or if it changes on repeated examinations, and if so, to determine the cause for these changes. These children had come to the Cleveland Clinic, for various reasons. A very brief case history summary is given at the end. The glucose load was 75 gm. up to 16 years of age, 100 gm. after that. The blood sugar levels were determined by the Myer modification of the Benedict method, using 1 c.c. of blood for each determination. Charts 1 to 19 are all constructed on the same scale so that comparisons can readily be made.

First, we have to consider the question of whether a glucose tolerance test curve is stabile or labile. Table I is an analysis of these curves. Ninety per cent of the curves which were normal at start remained normal, and one case, or 10 per cent, later became diabetic. Of those showing a diabetic curve at start, 55.5 per cent continued the same, and 4 cases, or 45.5 per cent, later became normal. The author is well aware of the fact that this is too small a series for a basis of any definite *ex cathedra* postulations, but it does offer us a

TABLE I

CHANGES IN THE GLUCOSE TOLERANCE CURVE WITH REPEATED TESTS

AT START	NUMBER CASES	CONTINUED SAME	PER CENT	BECAME DIABETIC	PER CENT	BECAME NORMAL	PER CENT
Children							
Normal	10	9	90.0	1	10.0		
Diabetic	9	5	55.5			4	45.5
Adults							
Normal	56	45	80.3	11	19.6		
Diabetic	71	50	70.4			21	29.6

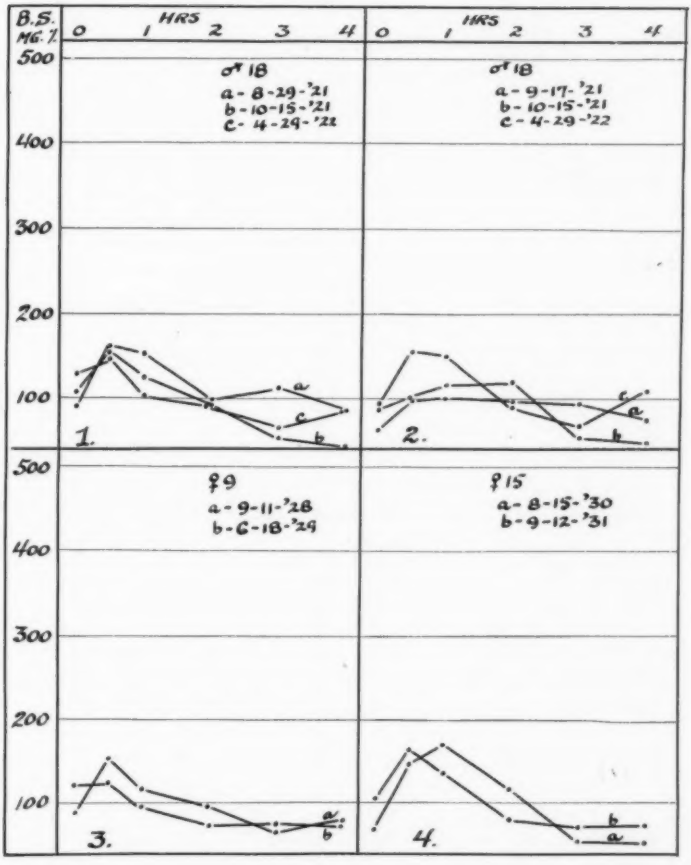
general lead. Similar studies on adults are included in the table for comparison. Here, as well as in the group of children, those who started out with normal curves and maintained them, the figures run fairly parallel. Where we meet with a deviation in these two groups is in the series starting with a diabetic curve. In the adults 29.6 per cent later turned normal against 45.5 per cent in the children. This fact would suggest that the curve in children is more labile than in the adults: that there are more factors, or else the factors which tend to disrupt temporarily the carbohydrate metabolism are more powerful, or more easily overbalanced than they are in later years. That these factors which tend to disrupt the carbohydrate metabolism are many can be seen from two lists following this paragraph. The problem of

endocrine disturbance plays a large part in some of these cases. Hypopituitary disease tends to give a low curve, and hyperpituitary disease gives a diabetic type of curve; hyperthyroidism, a high one; and hypothyroidism, a low one. A patient with hypothyroidism, given thyroid extract over a long period of time, may turn from a low normal curve to a frankly diabetic curve if the dosage of the thyroid extract has been excessive. What happens during the overmedication can well happen if the glands of internal secretion pass from a hypoactive to a hyperactive stage or vice versa. These factors must be taken into consideration in the evaluation of a glucose tolerance curve. A patient showing a diabetic curve, regardless of the cause, should be treated and watched until his carbohydrate metabolism has righted itself, as it will do in some cases. It is also true that some of the endocrine conditions which disturb the carbohydrate metabolism will right themselves even if we do nothing. This I have seen and shown in the cases of hyperthyroidism. The only question which can be raised here is: Taking two equal series of patients with disturbances of the carbohydrate metabolism due to endocrine causes, one treated and the other untreated, will the incidence of diabetes be the same in both series? This question I can answer by a positive "no." The untreated series will show a much larger incidence of diabetes. It is for this reason that we cannot afford to disregard an off-tolerance curve until we have assured ourselves that the metabolism has returned to normal.

Factors Which Tend to Show Improvement in the Glucose Tolerance Curve

1. Patient's going on a restricted diet; reduction of overweight.
2. Freak diet is likely to cause diabetic curve and return to a normal diet will show a normal curve.
3. Fear of diabetes if the test proper is likely to cause release of adrenalin into circulation increasing the blood sugar, and thus giving a false diabetic curve at the time, though on subsequent examinations curve will be normal.
4. Slow absorption of glucose from the stomach due to nausea which prolongs the absorption and lengthens the curve. If nausea is absent subsequently, tests may be normal. The characteristic dip in the curve between the first and second hour is the manifestation of this.
5. Performance of glucose tolerance test immediately before or after a major operation, when it is likely to show a distorted curve. Such tests should be avoided.
6. Any state of dehydration will show up a higher curve and will be therefore misleading.
7. Glucose tolerance test in prediabetics or diabetics toward the end of pregnancy will show an improvement.

8. A normal calorie diet, high in carbohydrates.
9. Thyroidectomy in cases of hyperthyroidism with disturbance of carbohydrate metabolism.
10. Possible periodic variation in the insulin output or the nervous mechanism involved.



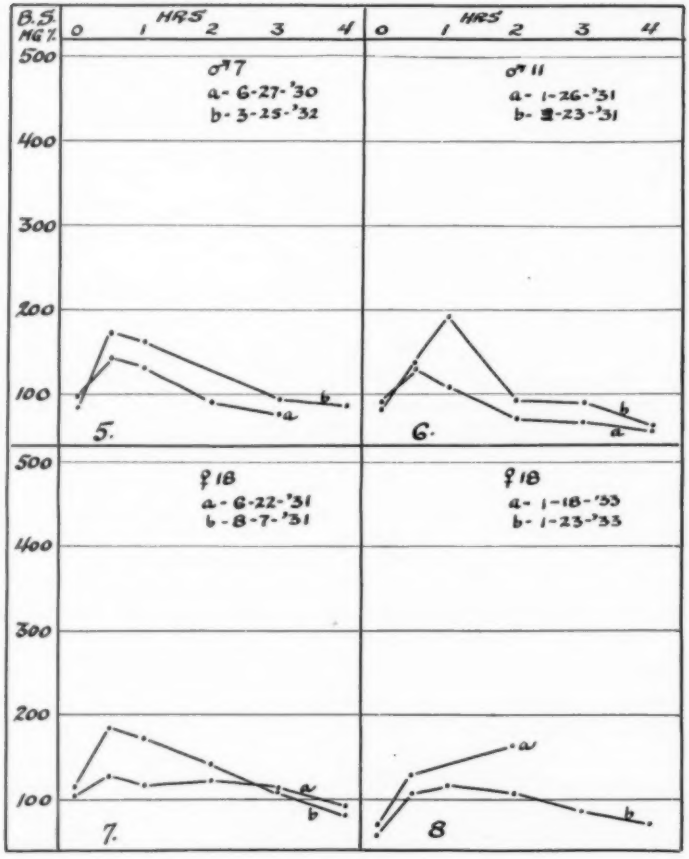
Charts 1-4.

11. The general or local increase in the alkalinity of an organism.
12. The use of alkalies (Underhill and Murlin).
13. Pyloric obstruction and vomiting.

Factors Which Tend to Make the Glucose Tolerance Curve Worse

1. A patient who starts with a prediabetic curve and continues to overeat.
2. Infections, especially flu.
3. A gradual disintegration of the pancreas from any cause.

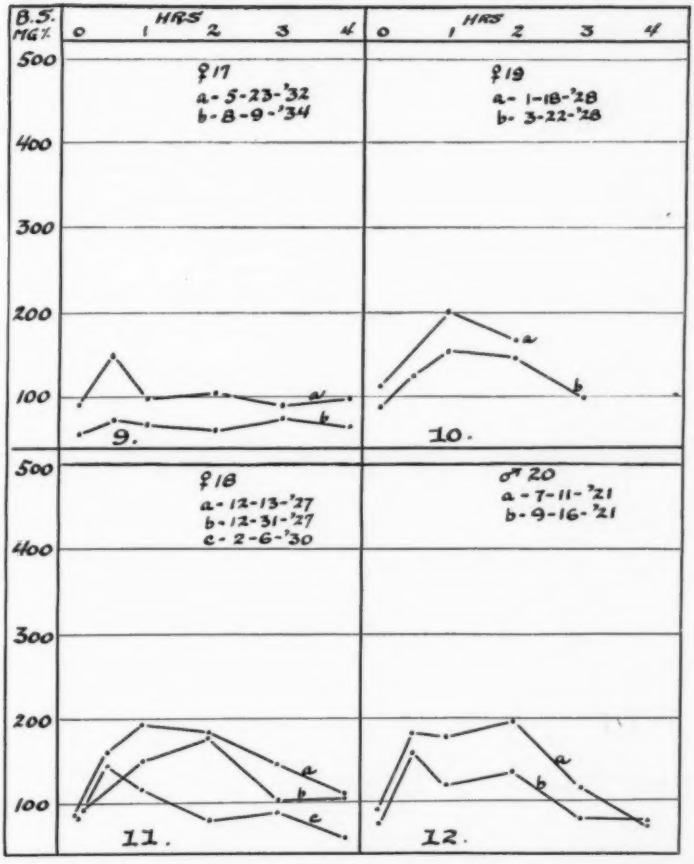
4. Any dieting preceding the test will give a false diabetic curve.
5. Diseases of the liver.
6. Hyperpituitary disease.
7. Hyperthyroidism in some cases.
8. Reaction following parturition, in mild diabetics or prediabetics.
9. Carbuncles.



Charts 5-8.

10. Obesity.
11. Anything stimulating the adrenals to overproduction of adrenalin.
12. Osteomyelitis and gangrene.
13. Partaking of acidifying diets thus causing slight acidosis.
14. Anemia.
15. Arteriosclerosis.
16. Circulatory failure.
17. Emotional upheavals.

Does a normal curve indicate that the patient's insulogenic reserve is such that he is absolutely protected from the development of diabetes? Again I have to answer this question with a positive "no." It is rare, very rare, to see a normal curve later turn diabetic, but it does happen. Let us take the Curve 16, for instance, which in 1933 was a frank diabetic curve. The child was placed on a diet, and one and a half years later when the tolerance test was repeated the curve

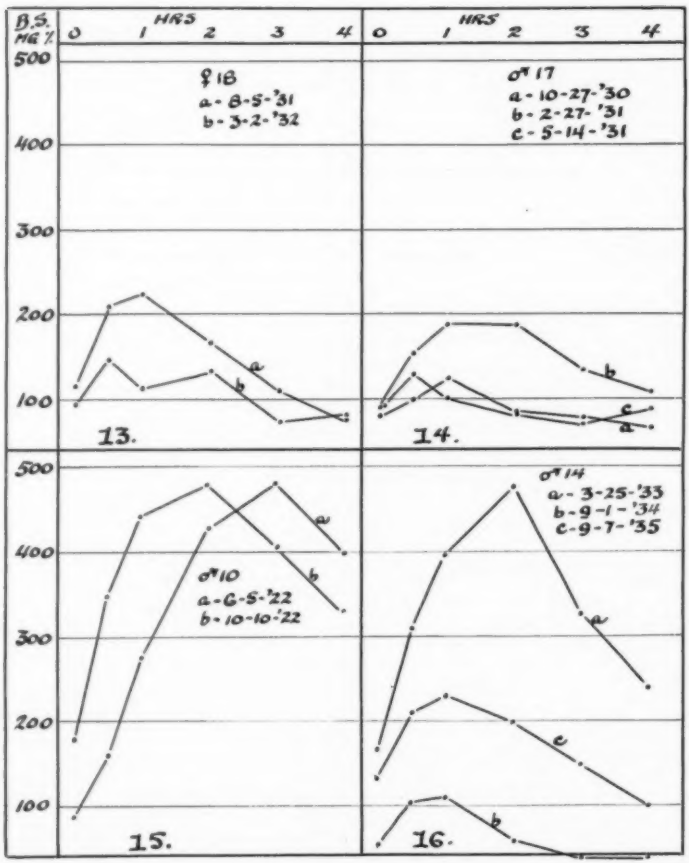


Charts 9-12.

was normal. He became careless, thinking he was cured, and ate everything. A year later a diabetic curve was the result. By this time enough damage was done to the pancreas that he was frankly diabetic and is now under treatment. Suppose a doctor had examined him in 1934 when he had a normal curve. He certainly would have thought that either an error occurred in 1933 or else the diagnosis of diabetes was a mistake. Only a prolonged observation would cor-

rect this opinion. It is for this reason that we teach "Once a diabetic, always a diabetic," even though there may be a marked improvement somewhere in the interim. Enough stress will break down this improvement in time.

I think that we can consider the glucose tolerance test as a fairly stable phenomenon if care is taken and the test done under standard conditions. There can be a change in the curve in later years, just as changes occur in the function of other organs. The pancreas is no exception.

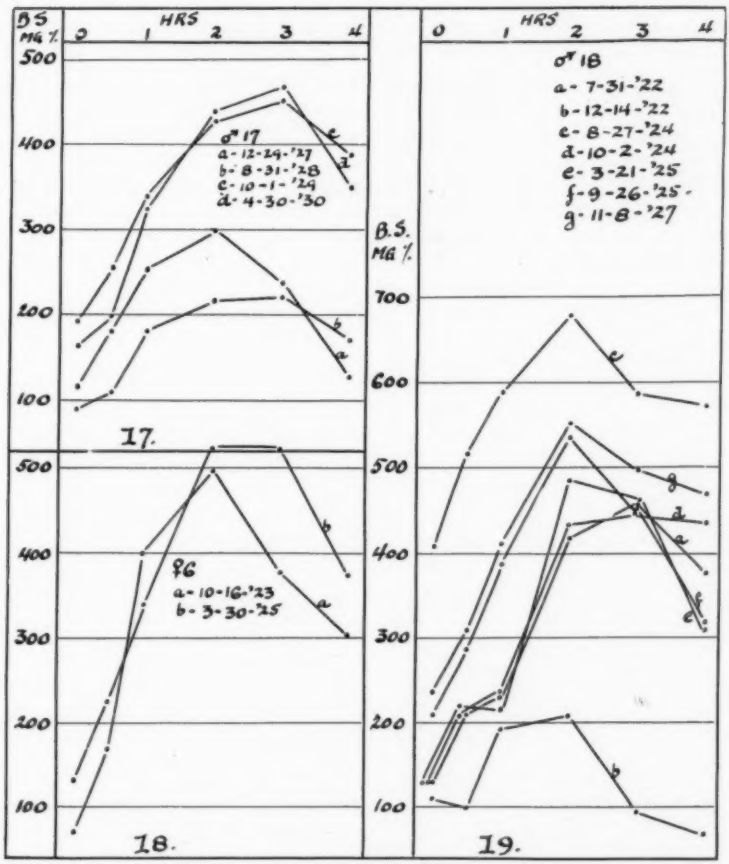


Charts 13-16.

BRIEF CASE HISTORIES

1. Male, 18. In perfect health. Normal weight.
2. Male, 18. In perfect health. Normal weight.
3. Female, 9. Glycosuria. Weight −12 per cent. Treated as diabetic because of glycosuria for 2 months. Father diabetic. Paternal grandfather diabetic.

4. Female, 15. Glycosuria. Weight minus 11 per cent. Blood sugar normal. Had glycosuria week ago. Losing weight. Paternal uncle diabetic.
5. Male, 7. Pituitary. Weight +20 per cent. Basal metabolic rate −23 per cent. Undescended testicle.
6. Male, 11. Hypothyroid. Blood pressure 95/55. Weight −12 per cent. Basal metabolic rate −38 per cent.
7. Female, 18. Blood pressure 152/90. Basal metabolic rate −18 per cent. Eye trouble. Drowsiness. Well developed and nourished. Improved on thyroid extract.



Charts 17-19.

8. Female, 18. Simmond's disease. Weight −53 per cent. Basal metabolic rate −25 per cent. No menstrual periods. Fatigue. Height 63.5 in. Hypogonadism.
9. Female, 17. Glycosuria. Blood pressure 112/74. Blood sugar normal. Weight −16 per cent. Large appetite. Menses regular.
10. Female, 19. Hypopituitary. Tendency to gain weight on low diet. Has not menstruated. Weight 140 pounds. Basal metabolic rate −26 per cent.

11. Female, 18. Petit mal. Adrenalectomy Dec. 23, 1927. Basal metabolic rate +7 per cent. Blood pressure 112/76. Weight −20 per cent.
12. Male, 20. In perfect health. Normal weight.
13. Female, 18. Pituitary dysfunction. Blood pressure 152/80. Obesity, weight +53 per cent. Basal metabolic rate −9 per cent.
14. Male, 17. Pituitary. Basal metabolic rate 23 per cent. Right frontal craniotomy Feb. 16, 1931, with evacuation of suprasellar cyst. Blood pressure 110/40. Weight −17 per cent.
15. Male, 10. Diabetic 2 months.
16. Male, 14. Glycosuria. Weight +19 per cent. Tonsillectomy in 1924. On regulated diet. Glucose tolerance became normal. Relaxed routine, diabetes reappeared, and continued to date.
17. Male, 17. Glycosuria. Weight −15 per cent. This boy never did show hyperglycemia on routine examination. Maternal grandfather diabetic.
18. Female, 6. Pneumonia in 1922, diabetes followed shortly after. Enlarged abdomen.
19. Male, 18. No diabetic history. Appendectomy in 1911. For a month classical symptoms of diabetes. Marked improvement in short time (see glucose tolerance, chart 2). Went to Europe, careless of routine, symptoms reappeared. Severe diabetic to this date.

CEREBRAL VASCULAR LESIONS ACCOMPANYING SICKLE-CELL ANEMIA

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ALTHOUGH the subject of sickle-cell anemia has been studied from many aspects, comparatively few reports are to be found on the manifestations of the disease as it affects the vascular system. Cook[1] first published an account of neurological symptoms in a negro boy, aged 7 years, who had sickle-cell anemia. Evidence of a subarachnoid hemorrhage associated with cerebral softening was noted at autopsy. Cook apparently considered the conditions coincidental. Two negro children with sickle-cell anemia, who had had vascular accidents resembling those seen in adults, were reported from the Duke Hospital.[2] Both recovered except for a residual spastic hemiplegia. At that time the question was raised as to the possibility of both of these children having thrombi of the cerebral vessels due to the sickling of the red cells, similar to those which occur in the spleen. Cooley[3] and Sydenstricker[4] have seen similar vascular accidents in three patients with sickle-cell anemia. Ford[5] mentioned the fact that several negro children with thrombosis of the dural sinuses also had sickle-cell anemia, but he did not emphasize the significance of the sickle-cell anemia as a possible etiological factor. He reported the autopsy findings on a negro boy 18 months of age with sickle-cell anemia, who suddenly began vomiting, developed a diplegia, and died two days after the onset. Post-mortem examination revealed a thrombus in the superior longitudinal sinus with softening and hemorrhagic infiltration of the superior frontal and parietal lobes of the hemispheres. These changes extended almost to the fissure of Sylvius. There was also hemorrhage in the subarachnoid space over the superior and lateral surfaces of the brain which had spread to some extent into the basal cisterna. Kampmeier[6] reported the case of a negro boy 10 years of age with sickle-cell anemia who had repeated attacks referable to the central nervous system, in the last of which there was hemiplegia. The patient recovered except for a residual spasticity on the right side. He emphasized the fact that pathologic changes characteristic of sickle-cell anemia permitted the diagnosis of cerebral thrombosis in his case. In a recent paper Yater and Hansmann[7] presented further evidence that the vessels of the central nervous system may be involved in sickle-cell anemia. They reported the autopsy findings of a negress, aged 38 years, with sickle-cell anemia, who had

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hypertrophy and failure of the right side of the heart due to thrombotic occlusions of the small and medium-sized arteries of the lungs, but presented no neurological symptoms. However, sections of the brain showed blood in the meninges over the right hemisphere. A small area of softening about 1 cm. in diameter was found in the cortex in the left parietal region. The choroid plexus was uniformly shrunken and of ashen color, and in places appeared cordlike. Gross serial sections of the spinal cord revealed small petechiae in the nerve trunks as they emerged from the cord to enter the dorsal root ganglia in the dorsal and lumbar regions. These authors also felt that although 50 per cent of patients with sicklemia have enlarged hearts, there is usually something other than the severe anemia responsible for the cardiac failure, namely, hypertension of the lesser circulation due to numerous occlusions of the medium-sized and small pulmonary arteries. Harden[8] has described vascular changes in the retina as well as extremely tortuous and thickened superficial temporal vessels in two negro children with sickle-cell anemia.

We have seen the following five patients with sickle-cell anemia who have had vascular accidents. Autopsy in one of them substantiates the diagnosis and clarifies the relationship of the two existing conditions.

CASE REPORTS

CASE 1.—A 6-year-old negro boy entered Duke Hospital on Aug. 13, 1933, because of headache, dizziness, and unconsciousness. He had been well until two days before admission. At that time, he complained of stomachache, which disappeared after catharsis. The next morning his head ached, and shortly afterward he became dizzy and drowsy, and was too weak to climb into bed. His left arm and leg made spasmodic movements and his right limbs were powerless. Speech was only slightly impaired until later in the day, when he became stuporous. He had taken no food or water for twenty-four hours preceding admission to the hospital. The family history was interesting in that a brother had died several months previously with a similar illness. A sister, aged 12 years, had had "rheumatism" for several years, and her blood smears showed 25 per cent immediate sickling. Smears of blood from the father and mother did not contain any sickle cells.

Physical Examination.—The boy's temperature on admission was 38° C. (100.5° F.); the pulse rate was 120; the respiratory rate was 28; and the blood pressure was 140 systolic and 75 diastolic. The patient was well developed, moderately dehydrated and in a semistuporous state. The skin was dry, and there was general glandular enlargement. The nail beds and mucous membranes were pale, while the sclerae were a deep greenish yellow. The tonsils had enlarged crypts and were moderately injected. There was a systolic murmur heard best at the apex and transmitted into the axilla. The right arm and leg were very weak and flaccid. The deep reflexes were hyperactive and the Babinski sign was present on both sides, but remained permanent only on the right side. The examination was otherwise negative.

Laboratory Tests.—Hemoglobin, 9.8 gm. (64 per cent Sahli); red blood cells, 2,740,000; white blood cells, 17,450; polymorphonuclear leucocytes, 80 per cent; large lymphocytes, 8 per cent; small lymphocytes, 8 per cent; myelocytes and transitionals, 4 per cent. There was 25 per cent immediate sickling, and 75 per

cent within four hours. Bleeding time was one and one-half minutes, and clotting time, one minute. Examinations of the stool and urine and intradermal tuberculin (0.1 mg. with old tuberculin), Wassermann and Schick tests gave negative results.

Course.—Immediately after the patient was admitted to the ward, a lumbar puncture was done and bloody fluid obtained. The spinal fluid was grossly clear the next day, but numerous red blood cells were found microscopically. The Pandy, tryptophan, and indole tests were negative. The patient remained in a semistuporous condition, and the right arm and leg became spastic. Seven days after admission, a cisternal puncture revealed many crenated and sickled red blood cells in the spinal fluid. The patient gradually became less stuporous and more aware of his surroundings. Later he began to talk and improved steadily. However, three days before discharge (six days after admission) right facial weakness developed. The eye grounds remained normal. He returned to the dispensary at intervals of every few months and, except for residual spastic paralysis of the right side and right facial weakness, his general condition has been much improved.

CASE 2.—J. G., a 6-year-old negro boy, was first seen at Duke Hospital on May 26, 1936, because of paralysis of the right side, which occurred two days previously. Since the age of two years he had attacks of petit mal. The family and past histories were otherwise noncontributory.

Physical Examination.—The temperature, pulse and respiration were normal. The blood pressure was 100 systolic and 60 diastolic. The boy was underdeveloped and poorly nourished. He had a papulopustular eruption over the trunk, legs, and arms. The mucous membranes were pale. The teeth were dirty and carious. The tonsils were enlarged, and the pharynx was reddened. The heart was enlarged, and a blowing systolic murmur could be heard over the entire precordium. The spleen was palpable. Neurological examination revealed weakness of the right arm and leg, right facial weakness, deviation of the tongue to the right, hyperactive deep reflexes, and a positive Babinski reflex on the right. There was no sensory impairment.

Laboratory Tests.—Hemoglobin 8.2 gm. (53 per cent Sahli); red blood cells 2,200,000; white blood cells, 16,150 with 76 per cent polymorphonuclear neutrophiles. Fresh preparation of blood revealed 90 per cent sickling of the red blood cells in 24 hours. The urine, tuberculin, Wassermann and Schick tests were negative.

Course.—The patient was given a high vitamin and high caloric diet. Five transfusions were given in the course of nine days and his hemoglobin rose to 10.8 gm. (70 per cent). Except for the residual spasticity and facial weakness on the right he was much improved.

CASE 3.—R. L., a negro boy 10 years of age, was seen with Dr. C. W. Purcell (Danville, Va.). At the age of 6 years he had a vascular accident that left him with paralysis of the right side. His past and family histories were essentially negative. On physical examination he was found to be undernourished, weighing only 24.5 kg. (54 pounds). The anterior cervical glands were enlarged. The liver and spleen were two fingerbreadths below the costal margin. He had definite nystagmus in all directions. The fundi were pale; no exudate was seen. The deep reflexes on the right were hyperactive, and the Babinski was positive. He had sustained ankle clonus on the right.

Laboratory Tests.—Hemoglobin 7.8 gm. (50 per cent Sahli). The red blood cells numbered 3,390,000, 90 per cent of which assumed the sickle form by the end of four hours. The blood and spinal fluid Wassermann tests were negative.

Course.—Since the onset of hemiplegia he had been given iron and liver by mouth, but his hemoglobin has never been higher than 7.8 gm. (50 per cent). There has been only slight improvement of his residual paralysis.

CASE 4.—D. M., a negro boy, aged 4 years, was admitted to Duke Hospital on Dec. 29, 1937, because of paralysis of the right side of three weeks' duration. He had a sudden onset of headache and vomiting Dec. 7, 1937. At about the same time the mother noticed that he had weakness of the entire right side. He also had difficulty in swallowing, chewing and talking.

Physical Examination.—The temperature, pulse, respirations, and blood pressure were normal. The patient was well developed and nourished, alert, and cooperative. Over his entire body were discrete scars. The eye grounds were normal. The lungs were clear to percussion and auscultation. The heart was not enlarged, and no murmurs were heard. The spleen was palpable at the costal margin. Neurological examination showed almost complete spastic paralysis on the right and right facial weakness. The deep reflexes on the right were hyperactive accompanied by a positive Babinski.

Laboratory Tests.—Hemoglobin, 11.1 gm. (72 per cent Sahli); red blood cells, 3,920,000; white blood cells, 8,000 with a normal differential count. The examination of the stool and urine and intradermal tuberculin (0.1 mg. with old tuberculin) and Wassermann and Schick tests were negative.

Course.—The initial sickle-cell preparation on this child was negative. However, on the third hospital day the temperature rose to 38.3° C. (101° F.) and another preparation at this time showed 100 per cent sickling. Splenectomy was advised, but the parents refused permission for the operation. There has been no improvement in the anemia or degree of spasticity.

CASE 5.—A 4-year-old negro girl first entered Duke Hospital on Feb. 8, 1934, with a history of paralysis of three weeks' duration. At the onset the child suddenly became speechless, her mouth drooped and saliva drooled from it. Two weeks later the child lost the use of her right arm and leg. The family history was interesting in that three other siblings died with a similar condition. In one of these siblings sickle-cell anemia had been diagnosed in our clinic. This child died at home after having been followed in the Duke Hospital Clinic.

Physical Examination.—Temperature, 37.5° C. (99.5° F.); pulse, 100; respiration, 28; blood pressure, 105/65. The child could neither walk nor speak but could comprehend commands and questions. The tongue could not be protruded nor moved from side to side. The spleen was palpable 2 to 3 fingerbreadths below the costal margin. Paralysis, weakness, and spasticity of right arm and leg were present. Reflexes were hyperactive throughout, but more marked on the right side. Babinski, Kernig and Brudzinski reflexes were negative. The spinal fluid was normal.

Laboratory Tests.—A fresh blood smear showed 100 per cent sickling in four hours; hemoglobin was 7.8 gm. (52 per cent Sahli); white blood cells, 24,000. An indirect van den Bergh reaction was present (trace). The patient was discharged with a diagnosis of sickle-cell anemia with cerebral thrombosis in region of the left internal capsule.

In an interval of three and one-half years, during which time the patient was followed in the dispensary, the use of the right arm and leg returned, and speech improved almost to normal; however, finer movements with her right hand, such as writing, buttoning clothes, or holding table silver, could not be performed. A residual limp and dragging of the right leg persisted.

Three and one-half years after the first admission the patient was again admitted to the hospital. Fifteen hours previously the child suddenly covered the frontal region of her head with her left hand and cried out that her head hurt;

she immediately crumpled to the floor. Her respirations were labored. Both legs were paralyzed, and she was unable to speak.

Physical Examination.—Temperature 39° C. (102.2° F.); pulse, 120; respiration, 38; blood pressure, 150/100. A small, undernourished 8-year-old negro girl lay unconscious in bed with mouth and eyes open, breathing rapidly and irregularly. The lungs were clear. A soft, blowing systolic murmur was heard over the entire precordium but best over the mitral area. The eyes moved aimlessly at times but tended towards left horizontal deviation. The spleen was not palpable. Both arms were spastic, more so on the right. The left leg was relaxed. Supraorbital pressure caused purposeful movements with both arms in an attempt to knock away the examiner's hands, and the left leg became spastic. Tendon reflexes were hyperactive on both sides, more marked on the right. The abdominal reflexes were absent; Kernig and Babinski, positive bilaterally. Response to pain stimuli was present over the entire body.

Accessory Clinical Findings.—Hemoglobin, 6.7 gm. (40 per cent Sahli); red blood cells, 1,500,000; white blood cells, 50,000; polymorphonuclear leucocytes, 94 per cent. Sickling, 25 per cent immediately; 95 per cent in 24 hours. The urine showed a four-plus albumin and from 5 to 10 granular and cellular casts per high power field. Spinal fluid showed initial pressure 270 mm., bloody fluid, slight xanthochromia, and 30,000 red blood cells. The Wassermann and colloidal mastic tests were negative. The patient was restrained, placed in a dark room, and given sedation and an infusion of 2.5 per cent glucose. No change followed, and she expired quietly 15 hours later with a temperature of 41° C. (105.8° F.).

Necropsy.—The large subarachnoid cerebral arteries were found to have undergone a gradual obliteration with final complete closure through a pathologic process identical with that which results in occlusion of the splenic arteries. The spleen which was so markedly enlarged on the child's first admission was a fibrotic nodular mass weighing only 1.5 gm. The complete autopsy findings are being reported in detail.[9]

COMMENT

Thrombotic phenomena are important episodes in the life history of these patients, and obliterative vascular changes and thrombi are a part of the pathologic picture of sickle-cell anemia. The cause of the tendency to capillary engorgement and arterial thromboses is not definitely known. Diggs'[10] theory that the distorted shape of the red blood cells prevents their ready passage through the capillaries probably explains the general vascular stasis, which is aided perhaps by the tendency of these cells to agglutinate. The amount of sickling seen in fresh blood preparations does not represent the actual amount of sickling present in the circulating blood, since the oxygen content of the air tends to restore the shape of the erythrocytes. It has been observed[11, 12] that the degree of oxygen unsaturation plays a large role in the amount of sickling in vivo. However, further observations fail to correlate the relationship between the degree of anoxemia and the severity of the disease.[13, 14] There is also the possibility of an increase in the degree of capillary stasis and other factors such as fever and infections. In Case 4 although we suspected sickle-cell anemia, fresh smears failed to show the sickling until the patient's temperature rose to 38.3° C. (101° F.), at which time 100 per cent

sickling was found. Recently we have had the opportunity of following a 9-month-old negro male with sickle-cell anemia and lobular pneumonia. At the height of his fever of 40° C. (104° F.) he had 50 per cent sickling within four hours. Two days after his crisis, while his temperature was normal, only 5 per cent sickling could be obtained in the four-hour period. Although the sickle-cell trait is said to exist in about 5 to 10 per cent of normal healthy negroes without anemia, and, although this condition has never been known to develop into sickle-cell anemia, still one might assume that in the presence of infection and fever some acceleration of the powers of sickling with anemia may take place.

In considering the pathologic findings in the fifth case one finds the changes in the splenic and cerebral vessels to be quite similar.

Our five patients were between the ages of 4 and 10 years. Four of them were males. The spleen was definitely palpable in four of the five patients. In Case 5, although the spleen was readily palpable at the time of the first vascular accident, three and one-half years later, when the second accident occurred, it could not be felt. Obviously considerable destruction of splenic tissue had taken place during the interval between the cerebral attacks. Although the results from splenectomy in these patients are not at all favorable in the several reported cases in the literature, the removal of an enlarged spleen gives better results than the removal of a small one.[15]

Recently Bosselman and Kraines[16] reported the case of a 13-year-old negro boy with sickle-cell anemia who developed aphasia six years after he had had a splenectomy. They suggested the occurrence of multiple small cerebral hemorrhages as the most likely cause of the symptoms. Apparently splenectomy in this particular patient did not prevent a vascular lesion. Nevertheless, certain patients with sickle-cell anemia show constitutional symptoms which are not unlike those seen with other true hemolytic anemias, namely, hemolytic icterus and erythroblastic anemia. Cardiac hypertrophy and dilation are the result of the recurring anemia or thrombotic phenomena,[7] and we have seen marked retardation of skeletal growth in some of these children with sicklemia. Splenectomy has given dramatic results in correcting the deranged metabolism which interferes with skeletal growth and proper bone structure, especially in patients with congenital hemolytic icterus. Therefore, it would appear that splenectomy should be performed more often in children with sickle-cell anemia who have enlarged spleens and who show such marked constitutional symptoms.

SUMMARY AND CONCLUSIONS

In the course of a study of five cases of sickle-cell anemia it has been shown that sickle-cell anemia may first become manifest as a

disease through the appearance of signs and symptoms indicative of cerebral vascular disease. The clinical features in such cases lead to the diagnosis of either cerebral vascular thrombosis or intracranial hemorrhages.

The pathologic findings in one of the patients here studied establish the fact that in sickle-cell anemia the large subarachnoid cerebral arteries become occluded in much the same manner as the splenic vessels.

Capillary stasis due to distortion and agglutination of red blood cells and other factors such as fever and infections probably contribute to the tendency to capillary engorgement and arterial thromboses.

The removal of a large spleen in a child with a previous vascular accident and constitutional symptoms should be given a further trial.

REFERENCES

1. Cook, W. C.: J. Med. **11**: 541, 1930.
2. Arena, J. M.: Am. J. Dis. Child. **49**: 722, 1935.
3. Cooley: Personal communication.
4. Sydenstricker: Personal communication.
5. Ford, F. R.: Diseases of the Nervous System in Infancy, Childhood and Adolescence, p. 642, Springfield, Ill., 1937, Charles C. Thomas.
6. Kampmeier, R. H.: Arch. Neurol. & Psychiat. 36: 1323, 1936.
7. Yater, W. M., and Hansmann, G. H.: Am. J. M. Sc. **191**: 474, 1937.
8. Harden, A. S.: Sickle-cell anemia, Am. J. Dis. Child. **54**: 1045, 1937.
9. Bridgers, W. H.: The Pathology of Cerebral Vascular Lesions Accompanying Sickle-Cell Anemia, Am. J. Path. **15**: May, 1939.
10. Diggs, L. W., and Ching, R. E.: South. Med. J. **27**: 839, 1934.
11. Scriver, J. B., and Waugh, T. R.: Canad. M. A. J. **23**: 375, 1930.
12. Hahn, E. V., and Gillespié, E. B.: Arch. Int. Med. **39**: 233, 1927.
13. Dolgopol, V. B., and Stitt, R. H.: Am. Rev. Tuberc. **19**: 454, 1929.
14. Graham, G. S., and McCarty, S. H.: South. Med. J. **23**: 598, 1930.
15. Anderson, W. W., and Ware, R. L.: J. A. M. A. **99**: 902, 1932.
16. Bosselman, B., and Kraines, S. H.: Am. J. Psychiat. **94**: 709, 1937.

TUBERCULIN PATCH TEST

A Comparison With the Pirquet and Mantoux Tests

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THE tuberculin patch test was introduced in a commercially available form* in 1937 by Vollmer and Goldberger. They reported a high degree of skin sensitivity of this test in a group of tuberculous children. In 1938 these authors further reported on the close agreement of the patch test with the Pirquet test. Steward also reported a very high degree of agreement with the Pirquet test in tuberculous children.

Because of the relatively high incidence of tuberculous infection among colored children, we believed that the Pediatric Service of the Harlem Hospital would be a suitable place to study the routine applicability of the patch test.

MATERIAL AND METHOD

Patch tests were done on 257 children. No attempt at selection of cases was made. The population represented is largely an indigent group, over 90 per cent of whom are negro.

The patch test was applied in the manner described by Vollmer. Simultaneously the Pirquet test was done with old tuberculin (Department of Health of the City of New York). The patch test was removed in two days. On the third day both the Pirquet test and the patch test were read. If both tests were negative or if the two tests did not correspond, a Mantoux test was done with 0.1 c.c. of a 1:1,000 solution of old tuberculin (Department of Health of the City of New York). As one might expect, it was not possible to do the Mantoux test in all ambulatory patients because of parental objections and failure to return after the Mantoux test was made.

RESULTS

In 200 cases both the patch test and the Pirquet test were negative. In 44 cases both tests were positive. The degree of reactivity was usually identical, but in 10 cases a marked difference was noted. In

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*The patch tests were made available through the Lederle Laboratories Inc., New York, N. Y. These patch tests were of a weaker strength (about 50%) than those at present distributed by the company.

6 of these the Pirquet reaction was stronger. In the other 4 the patch reaction was more marked. In 13 cases there was disagreement between the patch test and the Pirquet test (Table I).

TABLE I

RESULTS OF PATCH, PIRQUET, AND 1:1000 MANTOUX TESTS IN 257 CHILDREN

		CASES	MANTOUX 1:1000	
			NEGATIVE	POSITIVE
Patch 0	Pirquet 0	200	60	3
Patch +	Pirquet +	44	Not done	
Patch +	Pirquet 0	10	2†	7*
Patch 0	Pirquet +	3		1*
		257		

*Chest X-ray positive in 1 additional case in which Mantoux test was not done.
†No clinical evidence of tuberculosis. Chest X-ray negative in one case.

The Mantoux test was done in 63 children in whom both the patch test and the Pirquet test were negative. The Mantoux test was negative in 60 children and positive in 3 children. Although the number of cases is small, we may conclude that the patch test showed about 95 per cent as many reactors as the 1:1,000 Mantoux test. Only 3 positive reactors were missed by the patch test.

In 10 patients the patch test was positive and the Pirquet was negative. The Mantoux test was positive in 7 of these cases and negative in 2. In one additional child the Mantoux test was not done because the chest roentgenogram showed a tuberculous lesion. There was no clinical evidence of tuberculosis in the 2 children with negative Mantoux tests. The chest roentgenogram in one child was also negative. The patch test was therefore more sensitive in 8 cases than the Pirquet test, whereas in 2 cases the patch test gave a false positive reaction.

The patch test was negative in 3 children who had positive Pirquet tests. The Mantoux test was positive in 1 of these children. In the second child the chest roentgenogram showed evidence of a tuberculous infection, and the Mantoux test was omitted. The third child did not return after the Mantoux test was done.

No general reactions were noted following any of these tests, nor were any of the skin reactions very severe. We found no difficulty in interpreting the patch test especially after some experience with it. Of the three tuberculin tests, the patch test is considerably simpler to do. There is a further factor that no pain is caused, and no "needles" are exhibited. A disadvantage to be reckoned with in young children is their tendency to remove the patch.

CONCLUSIONS

It seems that the patch test is about as satisfactory as the Pirquet test in routine tuberculin testing.

From our series one would judge that 95 per cent of the positive reactors are determined by the patch test as compared to the 0.1 mg. Mantoux test. Two children gave positive patch tests without evidence of pulmonary tuberculosis. These children had negative Mantoux tests. It is our impression that these were false positive patch reactions. With this reservation in mind we believe that the patch test is a satisfactory tuberculin test for general use.

REFERENCES

Vollmer, H., and Goldberger, E. W.: Am. J. Dis. Child. **54**: 1019, 1937.
Vollmer, H., and Goldberger, E. W.: Am. J. Dis. Child. **56**: 584, 1938.
Steward, W. Dean: J. PEDIAT. **13**: 510, 1938.

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ATROPINE INTOXICATION

Its Manifestations in Infants and Children

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PERHAPS no other drugs, except phenobarbital, are more widely used in pediatrics than belladonna and its derivatives. They are used for the treatment of enuresis, pylorospasm, refraction of the eye or treatment of various eye diseases, preoperatively to diminish secretion, for the treatment of the chronic postencephalitic Parkinsonian syndrome, and many other conditions. Although atropine usually is used with impunity, symptoms of intoxication occasionally occur. Unfortunately they are often unrecognized as being related to the administration of the drug, and fatalities may result. From 1930 to 1938 eight cases of atropine poisoning with two fatalities have occurred among 3,200 pediatric admissions at the Duke Hospital. Because of the unusual features of some of these cases they are reported in detail.

CASES

Case 1.—M. H., a 3-year-old white girl, was brought to the Duke Hospital because she had perforated the cornea with a pair of scissors. Prior to operation, 6 drops of a 1 per cent atropine solution were dropped into the eye, and 0.1 mg. of atropine was given subcutaneously. After the operation (conjunctival flap for corneal perforation) approximately 1.5 gm. of a 1 per cent atropine ointment were placed on the dressing next to the eye, and the child was sent to the ward at 11:20 P.M.

Laboratory examination showed the white blood count, 32,000; red blood count, 5,770,000; hemoglobin, 17 gm. (110 per cent Sahli); urine, one-plus albumin.

Course:

11:20 P.M. Returned to the ward; pulse 134, respiration 24, color good.

11:40 P.M. Temperature 39.8° C. (103.7° F.).

12:00 midnight. Restless, thirsty, and complaining of heat; pulse 160, respiration 20.

2:00 A.M. Restless, respiration shallow and rapid; respiration 54, pulse 168.

4:00 A.M. Vomited, slight flush, temperature 42° C. (107.6° F.).

6:00 A.M. Voided and had stool, nauseated; temperature 42° C. (107.6° F.), pulse 160, respiration 58.

8:00 A.M. Voided and had stool, vomited, body rigid, 0.3 gm. aspirin and alcohol sponge given; temperature 41.8° C., fell to 40.8° C. (107.2 to 105.5° F.).

10:00 A.M. Eight c.c. 10 per cent calcium gluconate intravenously and a continuous saline subcutaneous infusion given; temperature 37.8° C. (100° F.).

11:00 A.M. Vomited, responded poorly, 6 mg. pilocarpine given subcutaneously; pulse weak, temperature 38.5° C. (101.3° F.).

From the Department of Pediatrics, Duke University School of Medicine, and Duke Hospital.

12:30 P.M. Two hundred c.c. 10 per cent glucose given intravenously; temperature 39° C. (102.2° F.).

1:00 P.M. Respiration labored, pulse weak and irregular, condition very poor, vomited, chewing tongue, alcohol sponge given. Temperature 40.3° C. (104.5° F.).

2:00 P.M. Green watery stool, ice packs applied.

6:12 P.M. Expired.

Total amount of atropine administered was 18.1 mg.

Post-mortem examination revealed perforation of the anterior chamber of left eye covered by conjunctival flap; acute congestion of the posterior portion of left upper lobe of lung; cloudy swelling of liver and kidneys; injection of superficial blood vessels of brain.

CASE 2.—A 2-year-old negro boy was brought to the Duke Hospital because of a lye stricture of the mouth upon which a plastic operation had been done at another hospital. The morning of the operation, the patient was given atropine and morphine preoperatively, and atropine postoperatively in unknown amounts. About four hours after the operation the child had definite signs of pulmonary congestion and cardiac dilatation; he was transferred to Duke Hospital. At this time the temperature was 40° C. (104° F.); pulse, 180; respirations, 60; and blood pressure, 90/00. The child was dehydrated, and the skin was hot, dry, and loose over the abdomen. The pupils were contracted; the mouth showed signs of the repair operation; and the lips were dried and fissured. Respirations were rapid, and squeaks, wheezes, and râles were heard over both lungs. The heart was markedly enlarged to the left. No murmurs were heard. The abdomen was soft though slightly protuberant.

Laboratory examination showed white blood count, 14,000; hemoglobin, 14.4 gm. (93 per cent Sahli).

Course.—The child was placed in an oxygen box, and parenteral fluids were given. The temperature fell to normal, and the pulse to 120 by the next day. Within forty-eight hours the respirations fell to 40, sweating started, and by the third hospital day the heart had returned to normal size. The remainder of the stay was uneventful.

CASE 3.—D. J., a 3-year-old white girl, was brought to the Duke Hospital because of failure to develop. The past history and physical examination revealed that the child had never walked or talked, was mentally deficient, and probably had a patent ductus arteriosus.

Laboratory examination showed white blood cells, 15,000; red blood cells, 4,750,000; hemoglobin, 15.3 gm. (98 per cent Sahli); urine and Wassermann test were negative.

Course.—The pupils were dilated with 2 drops of 1 per cent atropine in each eye for ophthalmoscopic examination. At 8 P.M. the temperature was 37.1° C. (98.7°F.). At 12 midnight it had risen to 39.3° C. (102.7° F.), and the child became very restless. At 4 A.M. the temperature was 40.1° C. (104.1° F.), and the patient began to shriek and had a generalized convulsion. Respirations became very irregular and labored; the heart became weaker; and at 7 A.M. the pulse was barely perceptible. The child died shortly thereafter despite the use of caffeine and adrenalin. The total amount of atropine administered was 2 mg. (2 drops of a 1 per cent solution in each eye).

CASE 4.—K. M., an 8-month-old white boy, was brought to the Duke Hospital because of inability to hold his head up, failure to gain weight, and vomiting. The referring pediatrist reported that when given 0.064 mg. (gr. 1/1,000) atropine every three hours for the vomiting, the child developed a high fever after two or three doses.

Laboratory.—Red blood count was 3,760,000; hemoglobin, 11.2 gm. (72 per cent Sahli).

Course.—The patient's temperature on admission was 37.2° C. (98.9° F.). The child was given 90 c.c. of formula every four hours with 4 drops of a 1 to 5,000 solution of atropine sulfate (0.04 mg.) twenty minutes before each meal. The temperature rose to 38.5° C. (101.3° F.) at 4 A.M., 39.5° C. (103.1° F.) at 4 P.M., and ranged there for the next two days. During this stage the pupils dilated, and the face was flushed. Atropine was discontinued on the third hospital day, and the temperature fell to 38° C. (100.4° F.) twenty-four hours later, and to normal within another twenty-four hours. The remainder of the hospital stay was uneventful.

CASES 5 AND 6.—A. S. H. and M. M. H., white twins, ate three alophen pills shortly before lunch; about one-half hour later the children looked flushed, and the empty pill box was found. The children were then brought to the Duke Hospital, and their stomachs were washed out. The only symptoms were flushed skin and dilated pupils.

Alophen pills

Aloin	1/4 grain	16.0 mg.
Strychnine	1/80 grain	0.8 mg.
Belladonna	1/12 grain	5.0 mg. (or 0.05 mg. of atropine)
Ipecac	1/15 grain	4.0 mg.
Phenolphthalein	1/2 grain	32.0 mg.

CASE 7.—R. D., a 5-year-old white boy, soon after receiving atropine drops for refraction, had a reaction. The temperature rose to 38.6° C. (101.4° F.), the skin became flushed, and he became hyperactive. The child was put to bed, ice packs were placed on the head. During the next two hours, the temperature returned to normal, the flush disappeared, and he made an uneventful recovery.

CASES 8 AND 9.—A 4-year-old negro girl and her 2-year-old brother were given a broth made from jimson weed, which contains stramonium, the action of which is similar to that of atropine. Five hours later the children were brought to the Duke Hospital because they were stuporous and complaining of dizzy sensations. The temperature, pulse, and respirations were normal; the pupils were dilated and reacted poorly to light. A flush could not be seen. The children were screaming and irritable. The patients' stomachs were washed out, and fluids were "forced." Recovery was uneventful.

SOURCE OF ATROPINE

Belladonna, its refined extracts, and related drugs are derived from plants, several of which grow wild in fields and, when ingested, contain a sufficient amount of the drug to cause poisoning. In some instances death has resulted from eating them.[1]

Atropa belladonna	The "deadly nightshade," found in cultivation.
Datura stramonium	"Thorn apple," "Jamestown weed," "jimson weed," or "cocklebur," found generally throughout the United States.
Hyoscyanus niger	"Henbane," found in northern United States, rarely in the South.
Mandragora officinale	"Mandrake," found in cultivation.

Poisoning has occurred from eating cooked turkeys[2] and rabbits,[3] which apparently had been feeding on some of the above plants. The serum of rabbits has been shown to neutralize atropine,[4] and this may account for the apparently normal condition of the animals. In one instance fifteen girls had mild toxic symptoms from eating Thanksgiving turkey; a broth from the meat of the fowl later readily dilated the pupil of an adult.[2]

The most common source of poisoning comes from the use of 1 per cent ophthalmic drops (1 drop containing 0.5 mg. or $\frac{1}{120}$ grain). Poisoning has occurred in infants from the use of 2 drops of 1:1,000 solution (0.1 mg. [$\frac{1}{600}$ gr.] to the drop) of atropine sulfate.[5] Poisoning has also occurred from the use of the drug when given subcutaneously.

ACTION OF ATROPINE

In general the drug paralyzes the parasympathetic nerve endings and is antagonistic to the parasympathetic drugs. In small doses it stimulates and in large doses depresses all body functions. It speeds up respiration, reduces and may stop bronchial and other secretions, increases body temperature, produces a flushed skin, dilates the pupils, paralyzes accommodation, relaxes the intestines, and prevents overaction of the bladder muscles.

Amounts		*Action*
Mg.	Gr.[6]	
0.5	(1/120)	Slowness of pulse and very slight dryness of throat.
0.5 to 1	(1/120 to 1/60)	Dryness in mouth, often with thirst.
2	(1/30)	Pupils dilated, not quite immobile, increase of pulse rate.
3 to 5	(1/20 to 1/12)	Headache, dysphagia, alteration of voice, muscular weakness, and restlessness.
7	(1/10)	Considerable dilatation of the pupils, disturbance of vision.
8	(1/8)	Excitement and muscular incoordination more marked.
10	(1/6)	Apathy. Hallucinations of delirium; unconsciousness.

The figures above indicate the usual amounts which affect adults, except those who are hypersensitive to the use of atropine. The minimal lethal dose has been stated to vary from 80 to 130 mg. in adults, and around 10 to 20 mg. in children. Pilcher[4] gave 2 to 6 mg. of atropine to eight children, varying in age from 1 to 3 years, half of whom were feeble-minded, without causing toxic effects. Despite these figures, deaths have been reported in adults from the use of 2 mg.,[7] and in children from the use of 0.4 mg. of the drug.[8] The marked variation is well demonstrated by one child's ability to tolerate 16 mg. a day and another's reaction to 1 drop (0.05 mg.) of this same solution.[4]

The usual atropine sulfate solutions used are 0.5 and 1 per cent; in the former one drop contains 0.25 mg. ($\frac{1}{250}$ gr.) and in the latter

one drop contains 0.5 mg. ($\frac{1}{120}$ gr.) of atropine. Obviously the careless use of eyedrops may cause severe toxic manifestations in certain individuals.

TOXIC SYMPTOMS

"Hot as a hare, blind as a bat, dry as a bone, red as a beet, and mad as a hen," describes the more common reactions seen in poisoning due to belladonna and its derivatives. Other reactions occur, however, with sufficient frequency to call attention to them. Dryness, thirst, flushing, dilatation of the pupils, and impairment of vision are usually the presenting symptoms, followed by a burning sensation in the throat, difficult swallowing, nausea, sometimes vomiting, excitement, delirium, visual hallucinations, staggering gait, rapid pulse and respirations, retention of urine (atropine is eliminated principally through the urine), diarrhea, numbness of the extremities, depression, coma, and death. A leucocytosis of 12,000 to 17,000 often is present.[5-9] The onset may occur within ten minutes after taking the drug,[10] or as late as a month after its continued use.[11] Fever, which occurs[5] in about 10 per cent of children, has been unsatisfactorily explained, e.g., stimulation of the heat centers, suppression of sweating, paralysis of the heat-inhibiting centers, paralysis of the thermogenic inhibiting centers in the spinal cord, dehydration, pharmacodynamic action of the minute doses of atropine which excite the vagosympathetic system stimulating the secretory function of the glands, chiefly the thyroid, the resultant transient hyperthyroidism accelerating metabolism, and producing abnormal heat, and last by a hypersensitivity to the drug.

Dryness, meaning dryness of the mouth and throat, diminution of saliva, thirst, difficulty in swallowing, and a dry skin are produced by suppression of the glands of secretion, i.e., salivary, sweat, lacrimal, mucous, gastric, and pancreatic. These actions are localized in the receptive substance on the nerve endings and are mutually antagonistic to pilocarpine. The flush, red skin, and eruption are due to the dilatation of the cutaneous vessels. The other symptoms probably come first from stimulation of the higher centers (excitement, delirium, visual hallucinations, and staggering gait), and second from depression of the central nervous system (coma, convulsions, and death).

TREATMENT

Therapy is still unsatisfactory. Atropine in small doses is antagonistic to morphine, but, when used in larger quantities, its action on the higher centers becomes very similar to that of morphine in producing severe depression. Therefore, morphine should be used with great caution, or better not at all.

The parasympathetic drugs (pilocarpine, physostigmine, acetylcholine, and muscarine) are antagonistic to atropine and should be used in all cases of poisoning. The usual dose is 10 mg. of pilocarpine

repeated every half hour until the mouth is moist. The necessary amount is said to vary from fifteen to thirty times the amount of atropine that has produced the poisoning. It must be remembered that atropine paralyzes the nerve endings, and since the parasympathetic drugs act mainly through the nerves themselves, their benefit is doubtful, especially when large doses of atropine have been given. Cerebral stimuli should be given as in poisoning by morphine.

The extremely high temperature must be controlled by sponges, ice packs, cold enemas, and moist sheets. Fluids should be forced. The bladder should be catheterized for there is often urinary retention and there is the possibility of reabsorption of the atropine from the bladder walls. The stomach should be lavaged to remove any atropine that might be present. Strong tea or tannin solution or, if these are not available, a weak solution of iodine should be used to precipitate the remaining alkaloid in the stomach. Finely powdered charcoal may be used to adsorb the poison.

Sedation, if used, must be used cautiously for if the poisoning is severe enough, the added sedation plus the depressing action of the atropine on the higher centers will only aggravate the existing condition.

SUMMARY

1. Atropine, though used with impunity in varied conditions, may cause poisoning; it also occurs in wild plants in sufficient amounts to cause poisoning if they are eaten.

2. Poisoning has occurred in adults with doses of less than 1 mg.,[12] and fatalities with 2 mg. In children fatalities have been reported from 0.4 mg.

3. Four drops of a 1 per cent solution of atropine contain 2 mg. (1/30 gr.) of the drug.

4. Toxic symptoms: Hot, dry, flushed skin, dilated pupils, nausea, diarrhea, delirium, staggering gait, and coma.

5. Treatment consists of administration of parasympathetic drugs until the mouth is moist, copious lavage of the stomach, cerebral stimulants if coma is present, and catheterization of the bladder. High temperatures should be controlled by alcohol sponges, forced fluids.

REFERENCES

1. McNally, W. D.: J. A. M. A. **65**: 1640, 1915.
2. Seelye, H. H.: M. Rec. **45**: 14, 1894.
3. Firth, Douglas, and Bentley, J. R.: Lancet **2**: 901, 1921.
4. Pilcher, J. D.: J. Pharmacol. and Exper. Therap. **52**: 196, 1934.
5. White, P. J.: Am. J. Dis. Child. **37**: 745, 1929.
6. Sollmann: Manual of Pharmacology, Table from Schmiedeberg; Atropine Chart, ed. 5, p. 370.
7. Arnold: Baltimore Medical Journal, p. 169, 1871.
8. Burrenich: Ann. et bull. Soc. méd. de Gand., p. 288, 1891.
9. Benzing, R.: Monatschr. f. Kinderh. **24**: 509, 1923.
10. Axtell, E. R.: N. Y. Med. Rec. **51**: 146, 1890.
11. Kelynack, T. N.: Brit. M. J. **1**: 421, 1890.
12. Owens, S. M.: Lancet **2**: 443, 1890.

DIAGNOSIS OF CONGENITAL SYPHILIS

PATHOGNOMONIC CRITERIA

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IT IS of great importance that the diagnosis of syphilis, whether congenital or acquired, be certain before treatment is started because of the prolonged, expensive, and heroic specific therapy which is essential for its cure. In the case of acquired syphilis, an ordered procedure for absolute diagnosis has been developed and is in general use.[1, 2] In congenital syphilis, for reasons to be elaborated upon later, no comprehensive diagnostic code has been established. Diagnostic criteria vary greatly in different communities.[2-6] The purpose of this paper is to review and evaluate existing means of diagnosis and to attempt to formulate an outline of pathognomonic criteria.*

Before the era of treatment for syphilitic pregnant women, congenital syphilis among the infants born of these women was both common and severe. Stillborn and heavily infected premature babies were of frequent occurrence. In full-term infants snuffles and skin rashes soon developed; they ate poorly, failed, and died. It was the exceptional infant who remained healthy and did not manifest symptoms of his mother's disease. In 1924 routine blood Wassermann tests and appropriate treatment, when indicated, became the rule among the pregnant women presenting themselves at the Stanford University Maternity Clinic. During the preceding 12 years, 26 per cent of the 224 fetal deaths were caused by syphilis. In the following decade syphilis accounted for only 2 per cent of 162 fetal deaths. This experience indicated the profound effect of prenatal treatment on the incidence of the fatal forms of neonatal congenital syphilis. McCord's extensive experience[10] with living infants born of syphilitic women illustrates that severe infections are rare, mild infections uncommon, and complete freedom from infection, the rule, when proper prenatal treatment has been given. He states, "Regardless of the activity of the disease, sufficient ante-partum antisyphilitic treatment assures the woman a syphilis-free baby in 95 per cent of the cases." There can be no question of the profound effect of ante-partum treatment in preventing congenital syphilis.[7, 11, 12, 13] Moore[1] says: "Congenital syphilis is as nearly a preventable disease as smallpox."†

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*Most American and English authorities[1, 2, 7, 8] require proof of the presence of congenital syphilis before instituting treatment. The German authority Hoffmann[9] advocates treatment on suspicion "of all newborn children of mothers who are still infectious or in whom infection is suspected." Hoffmann[9] also recommends "that the wives of infected men receive a sufficiently energetic preventive treatment in order to avert familial syphilis, for in this way the infection of the offspring is precluded."

†As great an authority as Stokes[2] makes the disturbing, but fortunately unsupported, remark, that "our [maternal] treatment methods may be simply converting early infantile into tardive heredosyphilis."

Granted the profound benefits to the unborn infant of maternal treatment during pregnancy, it is of fundamental importance to know the *modus operandi* of the ante-partum antisyphilitic medication if the status of the infant is to be properly appraised. *Is infection of the fetus prevented or is an infected fetus "cured"?* Continuous bimetal treatment instituted before and continued throughout pregnancy in all probability prevents infection of the fetus. It is generally believed that the product of conception in an untreated syphilitic woman is not infected before the fifth month of gestation. Such embryos as have been examined up to this period of pregnancy have without exception appeared to be nonsyphilitic.[3] Thus it is apparent that treatment started before the fourth or fifth month of gestation prevents infection of the child. It has been shown that treatment given only during the last trimester of pregnancy increases the chances that the infant will be viable at birth and will develop no evidence of syphilitic infection.[7] A considerable, but indeterminate, number of such infants may represent instances of congenital syphilis "cured" in utero. If this concept that intrauterine treatment of the infected fetus results in a lasting biologic cure in some cases is correct, then one must face the reasonable possibility that other infants will be born partially treated and will present the difficulties of diagnosis which often surround the partially treated disease in acquired syphilis.*

The diagnosis of congenital syphilis, once concerned principally with severe and relatively easily recognized cases, has been rendered much more difficult as a result of the nearly universal use of ante-partum treatment in infected women.[3, 4, 6, 7] A more refined and judicious use of diagnostic methods is necessary now in order to identify the occasional mildly infected infant among the many syphilis-free babies born of treated syphilitic mothers. Coincident with the diminished frequency and severity of congenital syphilis, there must come a change in attitude toward the newborn babies of syphilitic women. Whereas previously the baby was properly considered probably syphilitic, now the infant may be regarded as nonsyphilitic until proved otherwise. At one time it was perhaps excusable to give antisyphilitic treatment to all babies born of syphilitic women; only the exceptional infant was unjustly exposed to the dangers and disadvantages of unnecessary treatment. Such an attitude now would be an injustice to most of the babies.

The diagnosis of bacterial disease is most satisfactorily established by identifying the causative organism. Lacking this criterion, one must rely upon specific and exclusive changes in the body tissues or fluids. In either proving or disproving the presence of syphilis, every case must be

*It does not necessarily follow, however, that the percentage of intrauterine "cures" will be the same as in cases of acquired syphilis receiving comparable amounts of treatment. This point will have to be illuminated by the results of prolonged follow-up study. There is reason to suspect that syphilis is more easily "cured" in utero than in any period of extrauterine existence. If this is shown to be true, then many infants whose cases are evaluated by the diagnostic criteria of Hoffmann[5, 9] are unjustly exposed to the hazards, expense, and discomfort of treatment.

judged on its own merits. "The diagnosis of syphilis must depend on the examination of the individual under consideration."[8] A definitely positive or negative diagnosis cannot be established in the individual case by statistical probabilities.

There are three main methods of investigation by which the unquestionable presence or absence of congenital syphilis in living infants or children may be definitely determined:

(1) bacteriologic examination
(2) serologic examination
(3) roentgenologic osseous examination

Clinical evidences of syphilis are purposely not included as of absolute diagnostic reliability. Jeans[8] states, "Few of the clinical manifestations of [congenital] syphilis are pathognomonic." Typical florid syphilis may be diagnosed by physical examination alone, but in such cases bacteriologic, serologic, or roentgenologic proof is also present. On the other hand, many syphilitic babies at birth show either no physical signs of the disease or only suspicion-arousing signs. The maternal history is valuable as a suspicion-arouser, but it cannot be relied upon for absolute diagnosis. The same remarks apply to the results of examination of the placenta. In florid syphilis the placental changes are often diagnostic, but in the physically negative syphilitic baby examination of the placenta will seldom give conclusive evidence for or against the presence of congenital syphilis.[14] McKelvey and Turner[7] found that in approximately 9 out of 10 cases in which there were syphilitic changes in the placenta, the child was syphilitic also, but only 19 per cent of these infants were viable at birth and in an even smaller fraction were evidences of syphilis in the child "masked."

Bacteriological Examination.—Unfortunately it is not often possible to find *T. pallidum* in living congenitally syphilitic children. When the spirochete is easily found, the infection is usually heavy, and the diagnosis is readily established by other means. Complete diagnostic reliance may be placed upon the presence of *T. pallidum* in dark-field preparations from skin lesions, but opportunities to examine material from open lesions in congenital syphilis are seldom encountered after the first few months of life. Material from mucous membrane lesions may contain *T. microdentium* or *T. macrodentium,* harmless spirochetes which must not be confused with *T. pallidum.*

Ingraham[15] has recently revived interest in dark-field examination of scrapings from the wall of the umbilical vein. In 6 of 8 stillborn syphilitic infants the examination revealed the presence of the spirochetes. Of 87 living infants born of syphilitic women but showing no evidence of syphilis on physical examination, the umbilical vein scrapings were positive in 19 cases. Seventeen of these 19 infants and 18 of the remaining 68, in whose cases spirochetes were not demonstrated in the scrapings, were all shown by other means (presumably serologic and

roentgenologic) to be actually infected. Thus a positive result from the scrapings of the wall of the umbilical vein in accordance with Ingraham's technique showed a 90 per cent correlation with the presence of syphilis, but the test was negative in about 50 per cent of the infected babies. A larger series than Ingraham's is necessary to establish definitely the reliability of a positive test in proving infection in the infant. Ninety per cent is probably too low a figure for the actual reliability of a positive result with this diagnostic method. Certainly, if facilities for this type of examination are available, they should be used at least in those cases in which infection of the infant is probable on the basis of maternal history and treatment.

Serologic Examinations.—There is overwhelming evidence that Wassermann reagin may be present in the circulating blood of newborn infants born of syphilitic mothers without the concomitant presence of spirochetes in the infant's tissues.[1, 2, 4, 7, 12, 13, 16, 17, 18] Presumably the reagin, by passive transference, crosses the placental barrier from the maternal to the fetal blood. Thus a nonsyphilitic newborn infant may have a positive blood Wassermann test. One effect of maternal ante-partum treatment, in our experience, has been an increase in the proportion of nonsyphilitic Wassermann-positive newborn infants.

A number of investigators have discontinued making Wassermann tests on newborn babies' blood because they deem the test "unreliable" in this age group.[16, 19] In 1936 we[17] showed that by titration the Wassermann test could be made roughly quantitative and that the quantity of reagin gradually fell to, and remained at, a subreactive level in nonsyphilitic Wassermann-positive newborn infants. Usually reversal occurs within two or three weeks,[17, 18, 20, 21] but it may take at least as long as 70 days (Case 1). The greater the amount of reagin, the slower is complete reversal.

In the asymptomatic syphilitic infant reagin may be entirely absent at birth, but it will be present within a few weeks or at most within four months. More commonly the first serologic test will be positive. The reagin responsible for this early positive test may be either maternal or fetal in origin or may be a mixture of both maternal transplacental reagin and native fetal reagin. In general, titers tend to be higher in infected than in uninfected infants. If the cord blood reagin titer exceeds by a wide margin the maternal level, one cannot escape on theoretical ground the probability that the infant is syphilitic. There is as yet not enough clinical support to consider this observation of pathognomonic significance. Serologic differentiation between the infected and noninfected newborn infants depends, in our present state of knowledge, upon an increase in the amount of the reagin in the infected baby.

Our experience subsequent to our original report has confirmed our findings. Rising amounts of serum reagin in the asymptomatic physically negative syphilitic infant, followed by the development of snuffles, an

ulcer of the umbilicus, and the finding of spirochetes in material from the nose and umbilicus, have been observed. Prompt healing followed treatment (Case 2). An unequivocal rise of the blood Wassermann reagin titer is, in our opinion, positive proof of syphilis. The diagnostic value of the quantitative Wassermann tests has been substantiated by Christie.[21*]

A newborn syphilitic baby may have a negative blood Wassermann test. In our personal experience such an occurrence is uncommon, but in other localities the seronegative syphilitic infants apparently constitute a frequently observed and diagnostically difficult problem.[3, 6, 13] We have never encountered an infant who was seronegative at two months of age and seropositive later. This coincides with the experience of Cooke and Jeans.[12] In a series of 273 cases of syphilis in children, Roberts[13] encountered 103 infants with negative cord blood Wassermann reactions. Twenty-seven of these infants had subsequent negative blood tests, but only two of these negative tests occurred after the fourth month. Thus Roberts states, "These observations seem to justify the conclusion that it is probable that an infant born of a syphilitic mother, reaching the fourth month of life without physical or serologic evidence of the disease will escape the infection." The fear has been expressed that a child may occasionally be continuously seronegative and physically negative for years and eventually develop "tardive" congenital syphilis.† No conclusive cases of this type have been recorded. This fear is perhaps to a large extent carried over from the pre-Wassermann era when the seropositive, physically negative case could not be diagnosed till clinical "tardive" syphilis developed. We may then state that in our present state of knowledge two consecutive negative blood Wassermann tests and one negative spinal fluid Wassermann test in an untreated infant six months of age rule out congenital syphilis. McKelvey and Turner[7] recommend periodic serologic tests for a year or two longer. At any time after the first four months of life, two consecutive properly done, strongly positive, blood Wassermann tests are absolute proof of syphilis. Most anticomplementary Wassermann tests occur in cases of syphilis. It is not improbable that congenital syphilis occasionally "cures itself." How often this occurs cannot be stated. Rarely, in older children or young adults who have never received any specific treatment, the blood is seronegative, and there are no physical signs of congenital syphilis except for typical Hutchinson's teeth. If the spinal fluid is like-

*Accumulating evidence seems to indicate that in the neonatal period the significance of the blood Wassermann test differs from that of the Kahn, Kline, or Hinton test. In the cases reported in 1936[17] and in subsequent examples of seropositive nonsyphilitic newborn infants, we have found the Hinton test to be positive much less frequently than the Wassermann test. Gregor and Dalton[18] observed about one-third as many positive Kahn and Kline reactions as positive Wassermann reactions in their seropositive nonsyphilitic newborns, and Roby[22] has reported that the Kahn test is frequently negative in nonsyphilitic babies whose cord blood Wassermann reactions are positive. We are not yet sure that slight hemolysis may not have played a part in our comparative results with the Wassermann and Hinton tests.

†As great an authority as Stokes[2] makes the disturbing, but fortunately unsupported, remark, that "our [maternal] treatment methods may be simply converting early infantile into tardive heredosyphilis."

wise negative, treatment should not be given. Because of the great specificity of the Hutchinson's tooth, spontaneously "cured" congenital syphilis may be diagnosed in these cases. However, less than 1 per cent of the 521 syphilitic infants and children between the ages of 2 weeks and 15 years seen in the twenty-year period from 1914 to 1934 at the Harriet Lane Home of the Johns Hopkins Hospital in Baltimore had negative blood Wassermann reactions.[23]

Roentgenologic Osseous Examination.—Disregarding for the moment the question of possible or probable specificity, it must be acknowledged that roentgenologic findings are necessarily a much less direct form of diagnostic evidence in a bacterial disease such as syphilis than is the identification of the living organism or the positive specific spirochetal serologic reaction. Pathognomonic significance can be placed only upon those roentgen changes which by histopathologic, serologic, or bacteriologic correlation can be shown to mean active syphilitic infection. Furthermore, the roentgenologic diagnostic evidence must be of such definite and unequivocal nature as to permit no great differences in individual interpretation. In this connection the following remarks from Cooley and Reynolds[24] are pertinent: "The use of the x-ray for diagnosis has by no means attained the status of an exact science. Its value in any particular study must depend on the interpreter's understanding of the physical characteristics and limitations of the method itself, and of the pathologic states in question and the physical effects to be expected from them. To attain the highest degree of accuracy in the reading of films requires a combination of knowledge of the roentgenologist, the clinician, and the pathologist, and either roentgenologist or clinician will be successful in proportion to his competence in all these fields. It is to be assumed that each of these several observers has made painstaking effort to qualify himself in these respects, and the fact that they so often fail to agree must be looked upon as evidence that we have not as yet learned to use the x-ray as an instrument of precision."

The diagnostic roentgenologic osseous changes in congenital syphilis have been most definitely defined in the English and American literature by McLean.[25] However, McLean himself did not look upon roentgenologic studies as of premier reliability. He states that it is not "suggested that roentgenology will ever assume the place now held by serology in the diagnosis of the disease," and further, "it is only by the correlation of clinical, serologic and roentgenologic observations that knowledge of congenital syphilis will be furthered." His thorough, critical, and widely accepted study concerned itself with 102 cases of congenital syphilis. That the average intensity of infection in his cases was great is shown by the mortality of 42.1 per cent. In 24 cases, the bones were examined histologically. In 96 cases in which serologic tests of the blood were made (mainly Kahn and Noguchi tests), the results were positive in 95, anticomplementary in 1, and negative in none. In only

17 cases (16.6 per cent) were clinical evidences of syphilis "masked." Hence McLean based his study on a group of cases of severe congenital syphilis. In only 2 of the 102 cases was a positive roentgenologic diagnosis made before the positive serologic findings were obtained. In one of these two, a positive blood test was obtained two days after the roentgenologic diagnosis was made. This certainly does not prove that bone changes actually preceded serologic changes. In the other case, an infant six weeks old, slight bone changes which were passed as "negative for osseous syphilis" by "an experienced roentgenologist" were present when the Kahn test was negative. At 10 weeks of age, the presumptive Kahn test was 4+, 4+, 4+. At 3½ months, roentgenologic examination showed a marked progression of the osseous changes. The early bone changes in the light of subsequent serologic and roentgenologic events were undoubtedly related to syphilitic infection in this case, but a positive diagnosis of syphilis could scarcely be made on the basis of these early minimal and possibly nonspecific bone changes alone.

On the basis of his experience, McLean listed ten types of roentgenologic osseous changes which he considered diagnostic "on roentgen evidence alone" of congenital syphilis in the first months of life:

"1. Well-defined saw-tooth metaphysis in well calcified bones
2. Deep zones (in the longitudinal axis) of submetaphyseal rarefaction
3. Multiple 'separation of epiphyses' with or without impaction in bones which are not rachitic
4. Bilateral symmetrical osteomyelitis of the proximal mesial aspects of the tibiae
5. Multiple circumscribed osteomyelitis of the long bones shown by the roentgen rays as patchy areas of rarefaction
6. Multiple longitudinal areas of rarefaction (osteomyelitis) in the shafts of the long bones, sometimes resulting in fractures
7. Destructive lesions at the mesial or lateral aspects of the metaphyses (foci of rarefaction)
8. Multiple areas of cortical destruction generally seen within a centimeter of the ends of the bones.
9. Double zone of rarefaction at ends of bones
10. Localized periosteal cloaking occurring in more than one bone."

These diagnostic criteria have been widely accepted since their formulation in 1931. Obviously bone changes as seen on the roentgenogram must have modest beginnings, and McLean recognized the nonspecificity of the earliest changes, i.e., increased density of the zone of temporary calcification, and mild or moderate degrees of proximal rarefaction.

Criteria 1, 3, 4, 5, 6, 7 and 8 are still accepted as pathognomonic. A very high degree of technical perfection in making the roentgenogram is necessary for clear and unequivocal demonstration of criterion 1. Simple increase in the density of the metaphysis is definitely not diag-

nostic of syphilis according to McLean. In criterion 7 the changes should be multiple and very definite.

There is perhaps some question as to whether criteria 2, 9 and 10 are sufficiently reliable to retain their pathognomonic significance. As for criterion 2 we feel, even on McLean's personally reported experience, that perhaps it should not be included in its present form as a sign by which a definite diagnosis of congenital syphilis can be made "on roentgen evidence alone." Minor and sometimes rather marked degrees of submetaphyseal rarefaction occur in anemia in infants and in other conditions in early life in which growth has been disturbed. There should be perceptible disturbance of bone architecture before diagnosing syphilis on this criterion. I would suggest that this criterion be changed to read: "Deep zones (in the longitudinal axis) of submetaphyseal rarefaction with perceptible disturbance of cancellous bone architecture." As in criterion 1, a high degree of technical perfection in making the roentgenogram is necessary to demonstrate this point unequivocally. The conditions of criterion 9 may be simulated occasionally by nonsyphilitic states and by two, spaced, antenatal or postnatal courses of bismuth.[26] An example of the changes of criterion 10 occurring in a nonsyphilitic infant in the second month of life is reported in a subsequent paragraph (Case 3). So for criteria 2, with suggested change in phrasing, 9 and 10, we desire diagnostic confirmation from serology, bacteriology or roentgenology (by definite progression of the osseous changes) before an absolute diagnosis may be made.

Several investigators have recently reported that changes in the skeleton occur with surprising frequency in seronegative and physically negative infants born of syphilitic women, and have concluded that the osseous changes as shown by the roentgenogram are not infrequently more delicate indicators of the presence of syphilitic infection than are serological findings. If these observations and conclusions, never anticipated by McLean himself, are conclusively shown to be true, they will revolutionize present-day concepts of the pathogenesis of congenital syphilis, and dim the apparent brilliance of the results of ante-partum prophylaxis.

In view of the fact that the case material of these recent astonishing reports is not comparable to McLean's case material, it follows that the conclusions of the latter do not necessarily apply directly to the former. Parmelee and Halpern[5] reported material which in their opinion showed a marked superiority of osseous changes over serologic findings in the diagnosis of congenital syphilis throughout the first year of life. They report that the roentgen examinations were "positive" in 95 per cent of the infected infants, whereas the serologic tests were positive in only 29 per cent. The paper contains no individual case reports, no reproductions of roentgenograms, no statement of minimum diagnostic roentgenologic signs, no correlation with maternal treatment, no reports of

spinal fluid examinations, and no necropsy proof. The report is based on the cases of 104 infants, 79 of which were properly studied at birth, 60 at six weeks, 35 at three months, 23 at six months, and only 8 at 1 year. Sixty-seven cases (64 per cent) were considered "positively infected." In the discussion at the end of the paper some light is thrown upon the probable source of error by the following statements: "The earliest manifestation is the thickened epiphyseal line with a narrow zone of rarefaction immediately shaftward in the metaphysis" and "if physicians become familiar with the roentgenologic signs of syphilis, they will find a surprisingly large number that do show some evidence of syphilis." Hence the minimum roentgenological change considered "positively" diagnostic was apparently "the thickened epiphyseal line with a narrow zone of rarefaction immediately shaftward in the metaphysis."

McLean warns specifically against accepting increased density of the zone of temporary calcification and mild or moderate degrees of submetaphyseal decalcification as diagnostic of congenital syphilis. He says, in referring to the former, "It has been my experience that the roentgenologist should be cautious about making a diagnosis of syphilis on this evidence alone." Of the latter, he states ". . . it does occasionally occur in conditions other than syphilis. . .," and further, "although the roentgenologist is willing to defer to serology and clinical manifestations for the diagnosis of syphilis in a case showing the aforementioned osseous changes . . . he cannot make an unequivocal diagnosis of the disease on this roentgen evidence alone." Even in syphilitic infants, these two changes, McLean states, "may not be due to any local action of the spirochetes, but to the systemic effects of the disease on the blood" and may thus be nonspecific. Caffey[26] has recently shown that maternal ante-partum injections of bismuth may produce dense fetal metaphyseal lines, another source of error for the unwary.

Another report worthy of comment is Ingraham's paper, "Roentgen-Positive Seronegative Infantile Congenital Syphilis."[27] He states that during the course of the study of 134 selected cases there were "only nine in which the diagnosis of congenital syphilis was suggested by routine physical examination and serologic study before the x-ray films revealed lesions in the bones. In this same group roentgenographic evidence of bone changes which have been described as characteristic of congenital syphilis was found in 49 cases (36.5 per cent) . . . in 26 cases (19.4 per cent) at six days, before discharge from the maternity division, and in 23 additional cases (17.1 per cent) at ages from 1 to 10 months." No statement is made to indicate what were considered to be minimum diagnostic roentgenologic signs, and there is no table or other record to show the results of *simultaneous* serologic and roentgenologic examinations in the group as a whole. Without these two bits of essential information, the paper loses much of its force; for the minimum roentgen

criteria may have been of such a minor nature as not to be acceptable as of established pathognomonic significance, and, if the serologic examinations were not made at about the same time as the roentgenologic examinations, it would be impossible to determine which developed first, diagnostic roentgen changes or positive serologic reactions.

There are eight illustrative case reports in this paper. Case 1 is that of a normal newborn infant used as a control. Case 2 is that of a syphilitic baby, seronegative at birth, roentgen-positive at three weeks of age, and roentgen-positive at three months. Apparently no Wassermann or other serologic test was made except at birth. It is quite possible that the serologic reaction was positive at the time the first roentgen examinations were made. Case 3 is that of an infant born of a woman who acquired syphilis when three months pregnant. She had received eight injections of neoarsphenamine in the latter part of pregnancy. The infant was seronegative at birth and had no further blood test till she was three and one-half months of age. At this time the serologic reaction was strongly positive and florid syphilis was apparent. At six days of age an osseous roentgenogram revealed slight suspicion-arousing nondiagnostic changes which at three and one-half months had progressed to extensive lesions. This case, like Case 2, merely shows that a baby who is seronegative at birth may be syphilitic. Since the mother's infection occurred during pregnancy, this infant should have had more frequent blood Wassermann tests. Case 4 is that of an infant whose mother was infected late in pregnancy and received no ante-partum treatment. The cord blood Wassermann reaction was positive. At six weeks of age the infant was seronegative. No further serologic tests were done till the infant was four and three-quarters months old at which time the reaction of the blood was found to be strongly positive. Roentgenograms at birth showed minor bone changes. At two and one-half months and at five months these changes had progressed to pathognomonic syphilitic lesions. Again in this case, the lack of simultaneous blood and roentgenologic examinations vitiates the conclusion that diagnostic bone changes preceded positive serologic changes. It is certain that this infant was infected either shortly before or at birth. Possibly circulating Wassermann reagin had passed the placenta from the mother's circulation before parturition and then disappeared before the infant's own reagin began to rise about six weeks later. We are not willing to accept the "narrow band of sclerosis at the distal metaphysis" and "narrow band of rarefaction proximally," which were noted at six days of age, as pathognomonic of syphilis even though the clinical probability that the infant was infected is overwhelming in a special case of this sort. In Case 5, it is not clear from the protocol whether the negative blood reactions were obtained at three months or at five months of age. Judging from the description, the bone changes were rather bizarre. There is no doubt that the infant was syphilitic. A negative blood test in a severely infected infant of this age is so remarkable that it would have been wise to have repeated the blood test to rule out any possible error. This case presents the most convincing evidence of the entire group, of the failure of serology to indicate infection, but even here the positive results of the dark-field examination and not the peculiar roentgenologic changes are the conclusive proof of infection. This infant may have had acquired, not congenital, syphilis, for the mother showed no evidences of infection. If this were the case, the positive dark-field findings were perhaps obtained during the early seronegative phase of acquired syphilis. In Case 6 the cord blood Wassermann reaction was negative. At three months the infant had florid syphilis; the Wassermann reaction was positive, and there were definite marked roentgenologic changes typical of osseous syphilis. This case merely shows that an infant with a negative cord Wassermann reaction may have syphilis. Since the mother was known to be syphilitic and had received no

treatment during this pregnancy, the baby's blood should have been checked more frequently. In Case 7 the infant was not proved to be syphilitic although the mother was infected. The infant was seronegative at two months, at which time x-ray examination showed "marked flaring and sclerosis of the distal metaphyses of the radius and ulna bilaterally. There was periostitis on the outer aspects of both femurs and both tibias." This description does not correspond well with any of McLean's diagnostic criteria. Case 8 describes a congenitally deformed infant who died of pneumonia. Both mother and infant were physically and serologically negative. However, the description of the roentgenologic osseous changes in the infant seems to be characteristic of congenital syphilis. Without a postmortem examination report, the specificity of the bone changes may perhaps be questioned.

In another report appearing at about the same time as the one just discussed, Ingraham[6] presents the material in somewhat more detail. Especially worthy of comment is the table showing the effect of maternal treatment on the incidence of syphilis in the child. Syphilis was diagnosed in 48.2 per cent of the infants born of women who were treated for from four to eight weeks during pregnancy, whereas McKelvey and Turner[7] diagnosed syphilis in only 20.2 per cent of the offspring of women receiving the equivalent of three to six weeks of treatment (1 to 2 gm. of arsphenamine in 0.3 gm. doses weekly) during pregnancy. A relatively small part of this marked difference might be due to the difference in drugs employed, but this should be more than offset by the one to two weeks (approximately 30 per cent) longer periods of treatment of Ingraham's cases. In cases in which there was no prenatal treatment, Ingraham diagnosed syphilis in 79.8 per cent of the infants whereas McKelvey and Turner found 64.6 per cent to be syphilitic. In cases in which there were more than thirteen weeks of ante-partum treatment, McKelvey and Turner found no syphilis, whereas Ingraham diagnosed syphilis in three of twenty similar cases (15 per cent). So under all conditions of ante-partum treatment, but especially in the middle ranges, Ingraham diagnosed syphilis in the offspring much more frequently than did McKelvey and Turner. The difference is due primarily, I believe, to Ingraham's over-refined roentgen diagnostic criteria.*

Thus the reports of Parmelee and Halpern and of Ingraham do not, in our opinion, prove the superiority of roentgenology over serology in the diagnosis of congenital syphilis. In all three reports[5, 6, 27] an attempt has been made to attach pathognomonic significance to the earliest discernible roentgenologic changes in the bones. That these minor changes are often related to syphilitic infection is not to be argued, but at this stage the changes may be due to causes other than syphilis. They should certainly be looked upon as suspicion-arousing but not, in our present state of knowledge, as diagnostic signs. Whether or not the individual infant showing these changes is syphilitic will be proved by subsequent serologic, roentgenologic, or bacteriologic examination and occasionally

*The majority of Ingraham's and of McKelvey and Turner's patients were negroes from Philadelphia and Baltimore, respectively.

by physical signs. Repeated bone studies are less readily available than repeated serologic tests, and the results more equivocal; hence the serologic tests are in general more practical.

Our personal feeling concerning the probable significance of a little increased density in the zone of temporary calcification and/or slight or moderate degrees of submetaphyseal rarefaction in the long bones of young seronegative and physically normal infants born of syphilitic women is as follows:

(a) The changes will occur occasionally in infants born of nonsyphilitic women.

(b) In cases of infants whose mothers have received moderate or large amounts of ante-partum treatment, diagnostic evidences of active syphilis will seldom develop, and the changes in the bones will disappear within a few weeks. Perhaps these are cases of congenital syphilis "cured" in utero.

(c) In cases in which there has been no ante-partum antisyphilitic treatment a considerable number of the infants will within a few weeks be diagnosable syphilitics. The positive diagnosis will be more simply and conclusively demonstrated by blood tests repeated at ten-day intervals than in any other way.

There is still a need for two types of study: first, simultaneous serial roentgenologic and serologic examinations of newborn infants in whom syphilis is suspected and, second, investigation of the frequency and nature of roentgenologic bone changes in normal infants, and in various nonsyphilitic pathologic states during the first three or four months of life.

DISCUSSION

It is certainly not malpractice to insist upon a positive diagnosis before undertaking the treatment of syphilis. Indeed one of the important axioms of the proper management of this disease is that the diagnosis must be established before treatment is instituted. I have no argument with those who advocate treatment on strong or even on weak suspicion of the presence of the disease, but I do contend, in the interests of science and the advancement of our knowledge of the nature of the infection, that a sharp distinction should be drawn between a *positive* and a *presumptive* diagnosis of congenital syphilis. The use of the schema of diagnosis outlined in this paper (Tables I, II and III) will establish the presence or absence of syphilis in nearly all babies within three weeks after birth. Occasionally it will not be possible to make a positive diagnosis in an infected infant for a period of six weeks or two months after birth. Does this delay in instituting treatment in an apparently healthy but actually infected infant jeopardize the chances of ultimate cure? Although theoretically undesirable, there is no evidence that this amount of delay in such cases is harmful. There are perhaps occasional instances in infancy in which one would be justified in beginning treatment without the support of an absolutely positive diagnosis. Should such a situation arise, consultation with the best available authority in each of the fields concerned (roentgenology, pediatrics, and serology) should be obtained.

SUMMARY

Criteria accepted as diagnostic of congenital syphilis vary widely in different communities. There are many suspicion-arousing, but relatively few pathognomonic, circumstances, signs or symptoms of congenital syphilis. Pathognomonic evidence of the presence of syphilis in living infants and children is seldom afforded by the results of physical examination but is to be found in the results of properly interpreted dark-field, serologic and roentgenologic examinations. A critical analysis of the significance of the results of these diagnostic methods has led to the formulation of a tentative pathognomonic code as presented in Tables II and III. Table I offers a suggested chronological order of procedure for the recognition of syphilis in young infants. Three case reports are included to illustrate and emphasize the application and interpretation of certain diagnostic methods.

TABLE I

PROCEDURE FOR THE DIAGNOSIS OF CONGENITAL SYPHILIS IN YOUNG INFANTS

1. Routine Wassermann test, history (with syphilis in mind), and careful physical examination (with syphilis in mind) of all pregnant women at the time pregnancy is diagnosed. Frequent check-ups of suspicious cases.
2. Suitable treatment of every pregnant woman who has or has had syphilis, regardless of the results of serologic tests, physical signs of the disease, or previous treatment.
3. Dark-field examination of umbilical vein scrapings in every case in which there has been inadequate, irregular, or no ante-partum treatment.
4. Cord or peripheral infant blood Wassermann or other serologic test in every case and titrations in all positive cases. Without this original test, titrated when positive, it is impossible to evaluate properly the next test.
5. Roentgenograms of the long bones within two weeks after birth of those infants in which the presence of syphilis is fairly probable (inadequate, irregular or no ante-partum treatment) or in which the first serologic reaction was positive.
6. Repeated infant blood Wassermann tests at not longer than two-week intervals with titrations in cases in which the original test was positive.
7. Repeated roentgenograms at one month or six weeks of age in cases in which the diagnosis is still in doubt.
8. Repeated dark-field examinations of any suspicious lesions (mucous membranes of nose, mouth, or anus; diaper rash; slowly healing umbilical stump, etc.).
9. Spinal fluid examinations of infants in whom the presence of syphilis is fairly probable (see 5 above) when subsequent examinations have not revealed positive diagnostic results.

CASE REPORTS

CASE 1.—J. B., a girl, was born Dec. 4, 1934, at full term; the weight at birth was 2,820 gm. The mother stated that her mother and father had had syphilis; she herself was said to have been syphilitic at birth, but she did not receive treatment until she was 12 years old. In September, 1934, in the prenatal clinic, her Wassermann reaction was three-plus. She received thorough treatment for the remaining three months of her pregnancy, and she had no clinical evidence of syphilis and no history of distinctive lesions. The baby, though small, showed no evidence of disease, except that at the age of 15 days there was a small "macerated" area of excoriation on the perineum; this healed without specific treatment. Roentgenograms were made on Jan. 14, 1935 (age 6 weeks), and the bones of the arms and legs showed no evidence of syphilis. The results of Wassermann tests during the first three months of life are shown in Fig. 1.

TABLE II

TENTATIVE CRITERIA FOR POSITIVE DIAGNOSIS OF CONGENITAL SYPHILIS

I. Diagnosis established by dark-field examination (identification of two or more living *T. pallidum* in dark-field preparations)
  A. At birth
    1. In scrapings of the wall of the umbilical vein near the fetal end of the umbilical cord
  B. After birth
    1. In material from skin or mucous membrane lesions
II. Diagnosis established by serologic tests (properly done on suitable material)
  A. At birth
    1. High Wassermann reagin titer
    2. Wassermann reagin titer unequivocably greater than that of the maternal serum
  B. During first four months of life
    1. Negative test becoming positive
    2. Rise in titer on subsequent measurement of a positive serum
  C. After four months
    1. Strongly positive test (checked)
III. Diagnosis established by roentgenologic osseous examination (interpretation by a competent and experienced individual, preferably a radiologist)
  A. At birth
    1. Changes of the sort described by McLean's criteria 1, 3, 4, 5, 6, 7, and 8
  B. At six weeks or later
    1. Same as III, A, 1
    2. Definite progression of osseous lesions as compared with those seen at about the time of birth and reaching the stage of McLean's criteria 1, 3, 4, 5, 6, 7, 8, and 10.

TABLE III

TENTATIVE CRITERIA FOR ESTABLISHING THE ABSENCE OF CONGENITAL SYPHILIS IN UNTREATED INFANTS AND CHILDREN

I. At birth
  A. Nonsyphilitic mother
II. At four months
  A. Two negative blood and one negative spinal fluid serologic reactions, properly done on suitable material
III. After two years
  A. Two negative blood and one negative spinal fluid serologic reactions, properly done on suitable material

On May 15, 1935, the spinal fluid contained 1.1 leucocytes per cubic millimeter; the reactions to the Nonne and Noguchi tests were negative; the Wassermann reaction was negative; and the colloidal gold curve was 1111100000.

This infant has been examined physically for evidences of syphilis, and blood Wassermann tests have been performed at intervals, with uniformly negative results. The last serologic and physical examinations were done on March 8, 1937, when she was 2 years and 3 months old.

CASE 2.—This white male infant had three older siblings in all of whom the blood Wassermann reactions were negative. The father and mother were infected with syphilis when the mother was seven months pregnant, but their cases were undiagnosed and untreated until after the birth of this baby. The patient was born at term with no physical evidences of syphilis, but the cord blood Wassermann test was positive. Titration of the serum at 10 days showed a titer of between 10 and 19 units of reagin. At 12 days the umbilicus was noted to be raw "with a markedly indurated base." This may have been a chancre. Dark-field examination was not done. At 20

days the reagin titer was exactly 10 units, and the infant was still physically negative except for the umbilical lesion. At 50 days of age, nasal discharge had developed, and the umbilicus was still incompletely healed. The reagin titer had risen to between 20 and 40 units. Six days later the titer was exactly 40 units. At 69 days it was exactly 80 units. At this time spirochetes were found in the first examination of material from the umbilicus and nose, and a generalized lymphadenopathy was noted. The weight gain had been satisfactory. Treatment was instituted, and the lesions healed promptly. At the age of 120 days the reagin titer had fallen to 10 units (Fig. 2).

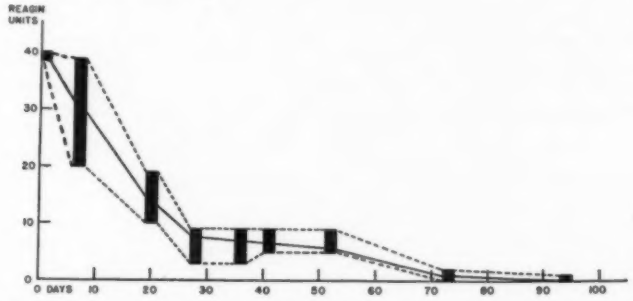

Fig. 1.—Case 1. Wassermann reagin titrations in a seropositive, nonsyphilitic infant. The black columns indicate possible range of reagin as determined by serum dilutions tested. The solid line approximates the probable true course of the serum reagin concentration; the broken lines indicate the theoretically possible maxima and minima.*

*See reference 16 for technique of estimating the serum reagin concentration and its expression in "units." Many closely graded serum dilutions are necessary in strongly positive serums to obtain an accurate estimate of the amount of reagin present. Theoretically, the smaller the difference between successive dilutions the more exact will be the results.

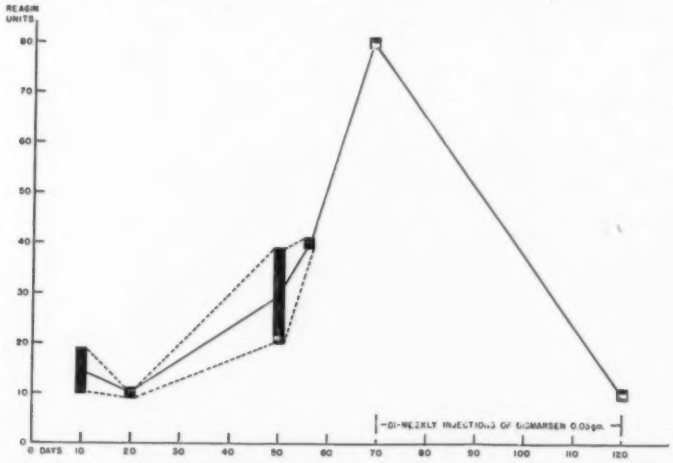

Fig. 2.—Case 2. Wassermann reagin titrations in a case of proved congenital syphilis. (See interpretation of Fig. 1.)

The first roentgenograms of the bones were taken at the age of 5 weeks. The long bones of the legs appeared normal, but slight changes were seen in the bones of the arms. There was a narrow dense white line across the distal ends of the radius and

ulna. Slight rarefaction of not more than 2 millimeters depth could be seen just proximal to the dense line at the lower end of the radius. The medial aspect of the shaft of the ulna showed a strip of periosteal density 1½ inches long and about 1 millimeter thick. Osseous roentgenograms were repeated at 4¾ months of age after 16 injections of 0.05 gm. of bismarsen had been given. There was considerable density at the ends of all the long bones, measuring as much as 6 millimeters at the distal ends of the femurs where it was most striking. This was interpreted as indicative of healing although it is possible that bismuth medication was responsible for some of the density.

Discussion.—The umbilical lesion, which may have been a chancre, probably would have yielded spirochetes when the infant was 12 days old, had the examination been made at that time. The rise of reagin to more than 20 units at 50 days of age was positive proof of syphilis. The bone changes which were apparent at 5 weeks of age were certainly syphilitic in character but they were not pathognomonic.

CASE 3.—D. S. was a colored female infant, born on Aug. 18, 1935, at full term. The mother had had, by a previous husband, four children aged 13, 8, 7, and 5 years. The first and third were physically and serologically negative for syphilis. The second and fourth had strongly positive blood Wassermann reactions; they had received no treatment and on physical examination showed no evidence of syphilis. The mother had negative Wassermann and Kahn blood reactions during this pregnancy. Several weeks after delivery her blood calcium was 12.1 mg. per cent, and roentgenograms of the pelvis showed normal bone structure. Nothing is known about this infant's father.

The baby was born at home. She was placed on an evaporated milk, water, and karo mixture. She gained weight, her skin was clear, and there was no nasal obstruction. She received a daily sun bath.

At 7 P.M. on September 25, when she was 5½ weeks old, one arm and leg twitched for 20 or 30 minutes. During the night the twitching recurred and involved other muscles. The free intervals became shorter and the attacks longer till September 29, when the spasmodic muscle contractions became continuous, and the baby was brought to the Children's Hospital of Philadelphia. On admission the rectal temperature was 99° F., the weight 8 pounds and 2 ounces. She was in a state of continuous clonic generalized convulsions. The fontanelle was normal, the skin clear, and the nose clean. She received two doses of 1 gm. of calcium gluconate intramuscularly, 3 gm. of calcium lactate daily by mouth, 15 drops of viosterol daily, and small repeated doses of phenobarbital. The convulsions gradually subsided in two days' time, but a positive Chvostek's sign and increased muscle tone persisted for two weeks.

The results of urinalysis, blood count, and spinal fluid examination were normal. The Wassermann and Kahn reactions of the blood and spinal fluid were negative. The blood calcium (after the two injections of calcium gluconate) was 8.2 mg. per 100 c.c. and the blood phosphorus was 5.8 mg. per 100 c.c. The blood sugar was 67 mg. per 100 c.c. On the second day after admission roentgenograms of the arms and legs showed a generalized periosteal cloaking of the long bones and marked osteochondritis at the proximal and distal ends of the left tibia and at the distal end of the right humerus. There were also scattered areas of less marked osteochondritis and submetaphyseal rarefaction. These changes were interpreted as characteristic of congenital syphilis by an experienced roentgenologist. No antisyphilitic medication was given. Eight days later (October 9) there was roentgen evidence of marked healing (Figs. 3 and 4), which was considered complete 3½ months later (Jan. 28, 1938), (Figs. 5 and 6). The blood calcium and phosphorus were 12.6 and 6.5 mg. per 100 c.c., respectively, on November 2, one month after admission. The blood Wassermann and Kahn tests were repeated every two weeks for

Fig. 3.—Case 3. Roentgenogram of arms at 7 weeks of age.

Fig. 4.—Case 3. Roentgenogram of legs at 7 weeks of age.

Fig. 5.—Case 3. Roentgenogram of arms at 5½ months of age. The cortex of the long bones is thickened, especially in the midpart of the diaphyses.

Fig. 6.—Case 3. Roentgenogram of legs at 5½ months of age.

two months and again at the ages of 5 and 31 months with uniformly negative results. The results of these tests were checked in other laboratories with the same negative findings.

Discussion.—This unique case demonstrates how contradictory, in the diagnosis of congenital syphilis, the serologic and roentgenologic findings may be. The convulsions were hypocalcemic in origin and were relieved by appropriate treatment. The extensive bone lesions healed, and the infant was physically, serologically, and roentgenologically normal at 5 months of age, without benefit of specific medication. At 2½ years of age the blood Wassermann test was negative, and physical examination revealed no evidence of syphilis.

Moore[1] speaks of the occurrence of "x-ray evidence of osteochondritis at birth in the absence of all other signs of syphilis" in infants born of syphilitic mothers treated during pregnancy. The bone lesions in these babies healed promptly, and no clinical or serologic evidences of syphilis appeared "during prolonged observation." Our case differs from these in that the mother received no prenatal treatment. Cregor and Dalton[18] mention three infants, born of treated syphilitic women, which showed roentgenologic changes in the bones suggestive of syphilis. The infants were not treated and remained physically and serologically normal during fifteen, twelve, and eight months of observation, respectively.

I wish to express appreciation to Dr. H. K. Faber for his encouragement and advice in the preparation of this paper and to Dr. R. R. Newell for his critical assistance in preparing the section on roentgenologic examination.

REFERENCES

1. Moore, J. E.: The Modern Treatment of Syphilis, Springfield, Ill., 1933, Charles C. Thomas.
2. Stokes, J. H.: Modern Clinical Syphilology, Philadelphia, 1928, W. B. Saunders Company.
3. Hoffmann, E.: J. Pediat. **9:** 569, 1936.
4. Dunham, E.: Am. J. Dis. Child. **43:** 317, 1932.
5. Parmelee, A. H., and Halpern, L. J.: J. A. M. A. **105:** 563, 1935.
6. Ingraham, N. R., Jr.: Am. J. Syph. & Neurol. **19:** 547, 1935.
7. McKelvey, J. L., and Turner, T. B.: J. A. M. A. **102:** 503, 1934.
8. Jeans, P. C.: Brennemann's "Practice of Pediatrics," Vol. 2, Chap. 26, Hagerstown, Md., 1937, W. F. Prior Co.
9. Hoffmann, E.: Am. J. Syph., Gonor. & Ven. Dis. **22:** 198, 1938.
10. McCord, J. R.: J. A. M. A. **105:** 89, 1935.
11. Cole, H. N., and others: J. A. M. A. **106:** 464, 1936.
12. Cooke, J. V., and Jeans, P. C.: Am. J. Syph. **6:** 569, 1922.
13. Roberts, M. H.: Am. J. Dis. Child. **45:** 461, 1933.
14. McCord, J. R.: Am. J. Obst. & Gynec. **28:** 743, 1934.
15. Ingraham, N. R., Jr.: J. A. M. A. **105:** 560, 1935.
16. Lemez, L.: Ztschr. f. Kinderh. **48:** 97, 1929.
17. Faber, H. K., and Black, W. C.: Am. J. Dis. Child. **51:** 1257, 1936.
18. Cregor, F. W., and Dalton, J. E.: Arch. Derm. & Syph. **35:** 580, 1937.
19. Williams, J. W.: Bull. Johns Hopkins Hosp. **31:** 335, 1920.
20. Davies, J. A. V.: J. Pediat. **13:** 341, 1938.
21. Christie, A. U.: Am. J. Dis. Child. **55:** 979, 1938.
22. Roby, J.: Health Bull., Dec., 1937, Rochester, N. Y.
23. Smith, F. R., Jr.: Am. J. Syph. & Neurol. **19:** 532, 1935.
24. Cooley, T. B., and Reynolds, L.: J. Pediat. **10:** 743, 1937.
25. McLean, Stafford: Am. J. Dis. Child. **41:** 130, 1931.
    Idem: Ibid. **41:** 363, 1931.
    Idem: Ibid. **41:** 607, 1931.
    Idem: Ibid. **41:** 887 and 1128, 1931.
    Idem: Ibid. **41:** 1411, 1931.
26. Caffey, J.: Am. J. Dis. Child. **53:** 56, 1937.
27. Ingraham, N. R.: Am. J. Dis. Child. **50:** 1444, 1935.

BRONCHOGRAPHY IN CHILDREN

A Simple Method Accomplished With General Anesthesia

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IN THE diagnosis of intrapulmonary conditions a bronchogram is frequently essential. An adult can usually be persuaded to submit to the instillation of oil under local anesthesia and will give the cooperation necessary to conveniently complete the procedure. With children, however, such cooperation is not readily obtained. Older children, especially those who have repeatedly been bronchoscoped, may submit to the instillation of lipiodol as readily as adults. Younger patients or those who are new in the hospital present difficulties which frequently are not overcome by any technique in current use.

The injection of oil through a large bore needle directly into the trachea by puncture through the skin of the neck is successful in many instances, but it has several serious objections. One is the frequent injection of oil into the peritracheal tissues which remains there indefinitely. Another is the occasional cellulitis developing at the site of puncture although this usually subsides without trouble. In one instance, however, the injection of oil into the peritracheal tissues was followed three weeks later by a retropharyngeal abscess and the child subsequently died from some form of respiratory obstruction. Autopsy not being obtainable, it was never determined what bearing the attempted bronchography had on the fatal outcome, but the feeling that it may have been an important factor caused us to abandon this procedure.

A review of the literature did not reveal a description of a method by which bronchography was accomplished with other than local anesthesia. It seemed advisable to investigate the possibilities of intravenous, rectal, and inhalation narcosis. The first important consideration was the selection of an anesthetic drug. It was imperative that the agent be nonirritating to pulmonary tissues, nonexplosive, sufficiently potent to obtund cough reflexes, simple to administer, and readily controllable. The possibilities of intravenous, rectal, and inhalation narcosis were investigated. The barbituric acid derivatives recommended for intravenous use were employed. It was determined that the anesthetic dose required to obtund the cough reflex of children closely approximated that dose which would cause respiratory arrest. Laryngospasm and bronchiolar spasm resulting from the parasympathetic action of these drugs make their use as anesthetics undesirable for bronchography.[1] Rectal anesthesia was employed without entire satisfaction. Dangerously large doses of rectal barbiturates or of avertin in amylene hydrate may not obtund

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laryngeal or cough reflexes. In our experience it was always necessary to complement their action. Rectal ether is advised because it minimizes the dangers from explosions but is undesirable since it does not reduce materially the effects of the drug upon inflamed respiratory passages. It was not seriously considered.

An effort was then made to adopt a technique whereby bronchograms could be completed during general narcosis. It was soon obvious that modifications of the standard accepted techniques were needed to meet all the requirements. Finally a method of anesthesia was devised which combined basal narcosis with avertin in amylene hydrate by rectum, the local application of metycaine in the pharynx, larynx, trachea, and bronchi, and the administration of nitrous oxide and oxygen, employing an intratracheal airway. At first glance this seems like an unduly complicated procedure, but actually, in the hands of a trained anesthetist, it is simple. When anesthesia is established, it requires but a moment to instill the lipiodol. Compared with the tedious and irritating wheedling necessary to anesthetize the larynx and instill lipiodol in a refractory and apprehensive child, it is a quick and pleasant method.

The procedure is accomplished by first giving the patient a cleansing enema not later than six hours prior to the scheduled time of study. One and one-half hours before anesthesia, premedication with an appropriate hypodermic dose of codeine and atropine or morphine and scopolamine is administered. Codeine gr. ¼ (0.015 gm.) and atropine gr. $\frac{1}{250}$ (0.00024 gm.) may usually be employed for the younger, undernourished and poorly developed children. For the older group (5 to 10 years) morphine and scopolamine is useful. The ⅛ gr. (0.0075 gm.) dose of morphine is never exceeded. A maximum of scopolamine gr. $\frac{1}{200}$ (0.0003 gm.) serves admirably to diminish secretions and complement the morphine effect by its psychic sedative action. Immediately before use, a 2.5 per cent solution of avertin in amylene hydrate containing 100 mg. per kilogram of body weight is prepared with distilled water. After testing the solution for acidity, an amount equal to 80 mg. per kilogram of body weight is instilled rectally from twenty to thirty minutes prior to the time the bronchographic study is contemplated. If at the end of fifteen to twenty minutes, satisfactory basal narcosis is not obtained, one-half of the remainder of the solution is given. That unused portion of the drug is utilized if 15 minutes after the second fractional dose the patient still reacts to slight painful stimuli. To diminish the still active pharyngeal and laryngeal reflexes and at the same time assist in eliminating the cough reflex, 1 to 3 c.c. of a 3 per cent metycaine solution is sprayed into the oropharynx under direct vision. Four to six minutes later the patient is anesthetized with nitrous oxide and oxygen, using the carbon dioxide absorption technique.[2] Nasal endotracheal intubation is then completed, if necessary under direct laryngoscopy. The distal 3 or 4 inches of the endotracheal tube is lubricated

with 3 per cent metycaine ointment. This not only acts as a lubricating medium, but complements the metycaine spray used to anesthetize the larynx and trachea. The nasal route for intubation is preferred since the tube passed through the small lumen of the nares remains fixed, and the unavoidable shifting which tends to stimulate the cough reflex is eliminated. The head and shoulders of the patient are now elevated approximately 15 degrees and not more than 1 c.c. of metycaine (3 per cent solution) is sprayed during inspiration into the endotracheal tube. After about five minutes anesthetization of the lower half of the trachea, carina, and proximal portions of the primary bronchi is complete. Anesthesia with nitrous oxide and oxygen is again induced. The patient is placed in the optimum position for the instillation of the contrast medium and the technical details for exposing the x-ray plates are completed. To prevent distortion of the plates by respiratory movements,

Fig. 1.—Bronchogram made by injecting lipiodol directly into the endotracheal tube, turning patient first to one side and then to the other. After the left side was filled, the movement of the endotracheal tube while changing the position of the child caused a cough which forced the lipiodol into the alveoli of the left upper lobe. By waiting a little longer for the metycaine to take effect the right side was successfully filled.

cessation of breathing is produced for the time required to complete the necessary bronchograms. This may be conveniently accomplished by rapid oxygenation and distention of the lungs immediately following deep nitrous oxide and oxygen anesthesia.

Immediately following the completion of the bronchograms removal of the major portion of the lipiodol is accomplished by means of a simple suction device. (Figs. 2 and 3.) By removing much of the lipiodol, subsequent coughing and the dissemination of infection to healthy portions of the lung parenchyma are minimized. Such suction may likewise be accomplished before the lipiodol is injected to remove excessive secretions

present. Obstruction to the contrast medium entering the smaller respiratory passages is thereby largely eliminated.

After this study was complete, a report was published which originated at Guy's Hospital, London.[3] In it Jacoby and Keats describe a method which employs basal narcosis with rectal avertin followed by open drop inhalation ether anesthesia. They recommend the method for its simplicity. The obvious objections to ether, namely, the harm that may

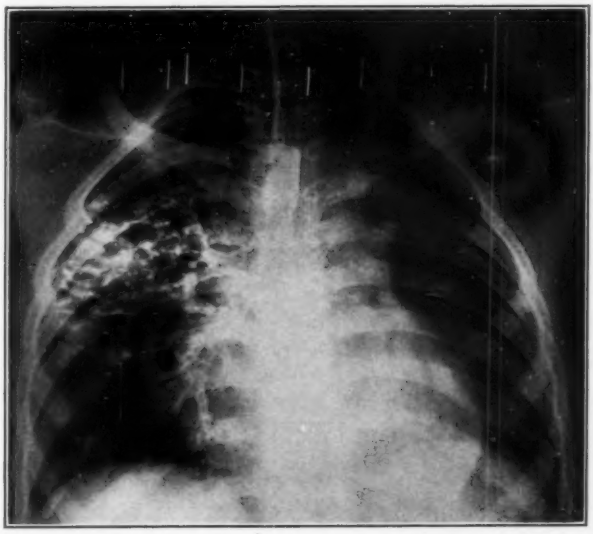

Fig. 2.—Injection of right upper and middle lobes by gravity. (The cuff of the endotracheal tube is filled with lipiodol instead of air.)

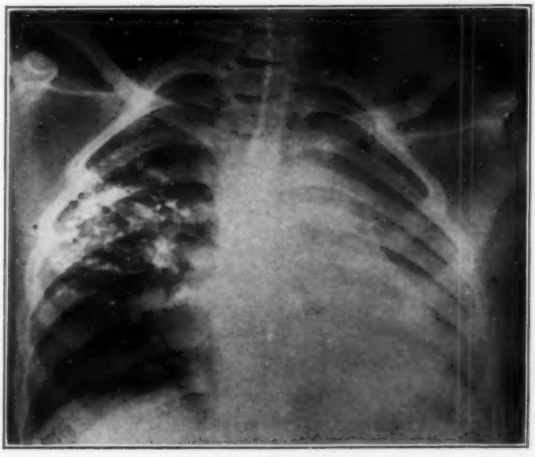

Fig. 3.—Same as Fig. 2 after removal of lipiodol by aspiration. Oil remains only in the bronchiectatic pockets.

result from its use for patients with existing pulmonary pathology and the dangers from fire and explosions in the x-ray room are not considered of enough importance to constitute a contraindication. They admit the safety and advantages of nitrous oxide-oxygen inhalation anesthesia but claim the technique for its use is too complicated. Our experience does not agree with the latter observation. The method described has not been found particularly complicated for one who has mastered the rather simple exercise of tracheal intubation. The safety with nitrous oxide as compared with ether far outweighs the added inconvenience.

Before instilling the lipiodol, certain anatomical features must be considered. In the normal individual the right main bronchus is almost a continuation of the trachea so that a straight instrument passed directly down the trachea will enter the right lung. If the instrument has sufficient flexibility and is passed farther, it will enter the lower lobe. The right middle lobe bronchus is given off anteriorly, and the right upper lobe bronchus is given off laterally. On the left side the left lower lobe bronchus is a direct continuation of the main bronchus. The left upper lobe bronchus is given off anteriorly.

The measurements of the bronchial tree are also of importance and are shown in the following table taken from Brunings and Albrecht.[4]

LENGTH IN CM. OF	CHILD 10 YR.	INFANT
Trachea	7	4.0
Right main bronchus	1	0.5
Left main bronchus	3	1.5
Right stem bronchus	2	1.0
Left stem bronchus	1	0.5
Upper teeth to trachea	10	8.0
Upper teeth to carina	17	12.0
Upper teeth to right lower lobe bronchus	20	13.5
Upper teeth to left lower lobe bronchus	21	14.0

The easiest method of instilling lipiodol and the one used most often is that by which the oil is injected directly into the tracheal tube (Fig. 1). This must be done slowly, for, if too much is instilled at one time, it will close the lumen of the tube temporarily and produce obstruction with cyanosis and coughing. While the oil is being injected, the head and shoulders of the child are slightly elevated and the body is turned so that the lung to be visualized is somewhat dependent. The lipiodol will then enter the lower lobe. If either of the upper lobes or the middle lobe are to be filled, the patient is placed in that position which will permit the oil to flow in the desired direction. For instance, if the right middle lobe is to be filled, the child is placed on his right side with head and shoulders slightly elevated while the oil is being introduced. After the oil has reached the right main bronchus (about one minute), the position is changed to the horizontal and the body rotated so that it is about three-quarters prone. This permits the oil to gravitate into the middle lobe. If the right upper lobe is to be examined (Fig. 2), the

initial introduction is the same, but, when the oil reaches the main bronchus, the head and shoulders are lowered below the pelvis to allow the oil to flow into the upper lobe. The left upper lobe is filled in a similar manner but with the child on the left side.

Obviously this method is not entirely exact and more than the desired area may often be filled, but it suffices in most cases. When a more accurate localization is required, the oil may be instilled through a No. 10 F whistle-tipped ureteral catheter. Such a catheter, graduated in centimeters, is passed to the desired part of the lung through the tracheal tube. This differs materially from the method used in adults by Goldman and Adams.[5] The Thompson bronchial catheter which they use would block the airway if passed through a tracheal tube in a child. A large ureteral catheter is essential since a smaller one offers too much obstruction to the passage of the unheated oil. The catheter can be bent at the end so that it may be made to enter either lung simply by rotating it and may even be made to enter a branch bronchus. Without fluoroscopic control, however, it is not always possible to be sure that a branch bronchus is entered, and it is much more difficult than the similar insertion of a Thompson catheter. The catheter is rotated so that it enters the desired main bronchus and is inserted the requisite distance for the tip to reach just beyond the point where the branch bronchus to be filled leaves the main bronchus. The child is then put directly in the position which will permit filling of the bronchus by gravity, and the oil is injected. To inject the oil a Luer Lok syringe with needle of sufficiently large caliber to fit the lumen of the catheter quite snugly is used. The injection of the unheated oil requires considerable force, and the leaks around the needle and catheter must be minimized. Heated oil gravitates into the alveoli quickly and does not outline the bronchus satisfactorily. The amount of lipiodol used varies with the size of the child and the extent of the bronchogram. As much as 5 c.c. has been needed for one lobe in a child of 3 years but seldom more than 10 c.c. for an entire lung in a child of 14 years. The instillation of too much oil is of little concern since it is always removed with a suction after the films have been exposed.

In a patient who has undergone lobectomy or pneumonectomy, the relation of main bronchus and trachea is changed so that the main bronchus of the side operated upon is more in line with the trachea and a straight tube will enter that side without guidance. If the right side has been operated upon, it may require considerable manipulation to get the catheter into the left lung. Fig. 4 is the bronchogram of a child who had a collapse of the left upper lobe and a lobectomy of the left lower lobe, the conditions being independent of each other. Lipiodol was injected through a straight fiber tube which is seen passing directly to the left side.

Coughing must be avoided as it tends to blow the lipiodol out into the alveoli, and the value of the picture for diagnosis is impaired (Fig. 1). After the tracheal tube is inserted, five minutes should be allowed for the anesthetic to take effect. The metycaine introduced through the tube should anesthetize the bronchial mucosa, but, if coughing occurs when the catheter is inserted, more metycaine should be injected through it to place the anesthetic directly on the bronchial mucosa. After the oil is injected through the catheter, it is better to remove the catheter before changing the position of the child. Movement of the catheter incident to manipulation of the patient may cause cough even when the bronchus seems well anesthetized.

Fig. 4.—Straight catheter passing directly to bronchus of operated side. In this instance the lower lobe had been removed and the upper lobe collapsed.

The use of a combination x-ray table and fluoroscope would greatly simplify the whole procedure as both could be used without shifting the patient, thus permitting greater accuracy in placing the catheter and filling the bronchus. When the patient is fluoroscoped on one apparatus and then shifted to another for exposure of the film, the procedure is not nearly as satisfactory. It is better to keep the child on one table and estimate the position of the catheter and the amount of oil required using the method described above, than to move the patient from one table to another.

The use of this method for more than a year indicates that it is a safe procedure and without sequelae of any consequence. In only one in-

stance was there any unfavorable reaction. This was a temperature rise to 101° F. accompanied by a few râles in the chest the day after bronchography. The fever and chest signs had entirely disappeared the following day.

SUMMARY

Methods commonly employed to complete bronchograms for children utilize local anesthesia in the conscious patient. Such procedures are not without danger, and good results are not always obtained. As a substitute method, a technique is described which utilizes inhalation anesthesia with nitrous oxide-oxygen, after basal narcosis with avertin in amylene hydrate and the application of 3 per cent metycaine solution to mucous membranes.

The method permits the accurate introduction of the contrast medium by way of an endotracheal tube and the removal of most of it after the completion of bronchograms.

Results after more than one year's trial indicate that the method is relatively safe, pleasant for the patients, and time saving.

The results with this procedure for completing bronchographic studies for children have been more satisfactory than with any other technique employed.

We take this opportunity to express our thanks to Miss Violet Vernon, formerly of the Bellevue Hospital x-ray department, for her helpful suggestions and valuable assistance.

REFERENCES

1. Burstein, C. L., and Rovenstine, E. A.: J. Pharmacol. & Exper. Therap. **63**: 42, 1938.
2. Rovenstine, E. A.: Surg. Gynec. & Obst. **63**: 325, 1936.
3. Jacoby, N. M., and Keats, G.: Lancet **2**: 191, 1938.
4. Brunings, W., and Albrecht, W.: "Direkte Endoskopie der Luft und Speisewege," Stuttgart, 1915, Ferdinand Enke.
5. Goldman, A., and Adams, R.: Ann. Surg. **106**: 976, 1937.

PECTIN-AGAR DIETS IN THE TREATMENT OF BACILLARY DYSENTERY OF INFANTS AND CHILDREN

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A CONTINUATION at the James Whitcomb Riley Hospital for Children of the use of the pectin-agar dextrimaltose product developed by several of us[1] has made it possible to study the cases of infantile diarrhea admitted to the hospital during the past three years. The high incidence of bacillary dysentery in this series seemed to offer an opportunity to report the use of this new dietary treatment in the type of case which must be considered as giving the crucial test for the efficacy of any therapy for diarrhea.

Much has appeared in the foreign literature on the use of the raw apple diet and apple powder in the treatment of diarrheal conditions of various types, but there have been comparatively few articles dealing with the use of this dietary treatment in infectious diarrhea. Moro[2] reported success in all but one case of 15 dysentery and dysentery-like cases in children from 2 to 10 years of age, while Wolff[3] observed 5 cases of true dysentery with innumerable mucous stools that showed excellent response to the apple therapy in twenty-four hours with decrease in tenesmus and fever, but the improvement was accompanied by a rapid loss in weight. Schreiber[4] and Mouzon[5] observed that the apple diet acted favorably on dysentery due to Flexner and Hiss-Y bacillus. Heisler,[6] Malmberg,[7] and Earnshaw[8] obtained excellent results in cases of epidemic dysentery while Hartwich[9] reported good results in 19 dysentery cases, 17 being of the Sonne type. Schlesinger[10] reported that patients severely ill with bacillary dysentery seemed to recover more rapidly with the apple diet than did other similar cases treated by the usual methods. However, he felt the patient's recovery was no guarantee that the dysentery bacillus had disappeared from the stools. Skinner,[11] in reporting an outbreak of epidemic dysentery in which the diplobacillus was thought to be the pathogenic organism, stated that the apple diet was not specific in any of these cases, but he felt that the marked improvement noted in some of the cases at the termination of the apple diet might indicate a use for this treatment as an occasional complete change of food, thus disturbing the habitat to which the organisms of the bowel were accustomed. In a report of 100 cases of acute dysentery in infants and children under 2 years of age in which the comparative values of human milk, protein milk, buttermilk, a carbohydrate diet and the Moro-Heisler apple diet were given, Sabri and co-

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This study was aided by grants from Mead Johnson and Company, Evansville, Indiana, and the Landon Research Fund.

workers[12] gave the results from the use of the apple or apple powder as being satisfactory but concluded, "Bacillary dysentery is a self-limited disease in which recovery depends upon the development of immunity on the part of the body. Until such immunity has developed the disease will continue its course irrespective of the character of the diet." Smith and Fried[13] observed that none of their dysentery cases treated with the apple diet showed any permanent improvement, but the level of feeding used by these workers in their cases was much lower than that generally advocated for the best results.

While many of these report good results in controlling the diarrhea, the low caloric value of these feedings, the difficulty in feeding the large amounts of apple necessary, the marked weight losses encountered, the difficulty in obtaining desirable fruit, and the trouble repeatedly reported in returning the patients to the normal diet without recurrences of symptoms were definite disadvantages to the apple therapy. It was also felt that the apple diet left something to be desired in producing formed stools.

The pectin-agar preparation was developed in an attempt to overcome the disadvantages of the raw fruit diets and at the same time to retain the good points and to eliminate the necessity of starvation which has always been a basic principle in all types of diarrheal therapy. Influenced by the experimental and clinical work of Malyoth,[14] Bauman,[15] and others showing that pectin and cellulose were the active agents in the apple therapy, a combination of pectin and agar-agar plus dextrimaltose was devised. Although the proportions have been changed several times the product as used the last 3 years was essentially:

Pectin	6.3%
Agar-agar	4.3%
Dextrimaltose	89.4%

These are mixed together in a powder,* which is used in the milk for the feedings of the infant or child suffering the diarrheal symptoms.

METHOD

Two basic forms of feedings have been found very practical. A fluid form which is used for the nurslings or for gavage purposes is made in the proportion of 1 cup of the pectin-agar powder to 24 ounces of milk, while for the older child who is spoon fed, the more concentrated combination of 1 cup of the powder to 16 ounces of milk is used. The milk is added slowly to the powder and the combination cooked in a double boiler 10 to 15 minutes with occasional stirring. The more fluid form is placed in nursing bottles in the quantity desired for each feeding. When cold, this forms a soft gel which upon reheating and shaking will break down into a smooth thick liquid and can be fed

*Kindly furnished by Mead Johnson and Company, Evansville, Ind.

through a nipple with an enlarged opening. The infants take the feedings as readily as do the older children. However, we have found that it is sometimes necessary to add flavoring such as chocolate, vanilla, or peppermint, or sliced bananas, banana powder, or various colorings to overcome the objections which were sometimes encountered with the older children. Some from this older group seemed to prefer the feedings warm, while others took them more readily if chilled or even frozen. During the first few years of the use of this product, while we were uncertain as to the extent of the therapeutic action of this material, we made the feedings with water, then very dilute milk mixtures, and later skimmed milk. However, during the last three years one-half skimmed and even whole milk have been used with equal success.

The pectin-agar feedings were ordered for the infants upon admission, and no starvation period was used. No other food was given by mouth except glucose water which was offered *ad libitum*. Complete bedside records were kept for each patient.* Daily weights, temperatures, amounts of fluids taken, frequencies and types of vomiting were charted. The type of formula, method of administration, amount of each feeding taken and how the child took the feeding, as well as complete stool records giving the number, consistency, quantity, color and the mucus, pus and blood content were kept. Supportive therapy was given as deemed advisable. To combat the dehydration which was present in some degree in practically every case in this series, fluids were given by mouth. However, in many cases insufficient amounts were taken or retained and when the normal urinary output could not be restored, parenteral routes were used. Glucose alternating with saline was given intravenously and in some cases subcutaneously; and, when more normal circulatory volume had been reestablished, one or two and in the severe cases even four or more small blood transfusions were given. Since anorexia was encountered in many of these severely toxic patients, it was often necessary to give the feedings by gavage. In cases with vomiting as a disturbing factor, the thick consistency of the pectin-agar feedings tended in the majority of cases to reduce the regurgitations; however, if the vomiting continued, it was sometimes necessary to give very frequent feedings of a more concentrated formula; in some very persistent cases the feedings were withheld for 12 to 18 hours and then resumed.

Proctoscopic examinations were made on every case possible. The rectum was flushed with physiologic saline solution, and a smear was taken directly from the bowel wall for examination. Stool specimens were taken on three successive days for culture, and all specimens were examined and cultured promptly after collection. During the summer of 1936 agglutination tests for the dysentery group were done routinely on admission and just before discharge; during the other two years agglutination tests were done only for the patients who were suspected of

*It is a pleasure to acknowledge the generous assistance of Nell Kolb, R.N.

TABLE I

RESULTS FROM PECTIN-AGAR TREATMENT

	1936		1937		1938	
	INFECTIOUS GASTRO-ENTERITIS	BACILLARY DYSENTERY	INFECTIOUS GASTRO-ENTERITIS	BACILLARY DYSENTERY	INFECTIOUS GASTRO-ENTERITIS	BACILLARY DYSENTERY
NUMBER OF CASES	6	19	17	15	4	18
NUMBER OF DEATHS		6	5	8		2
RESULTS OF RECOVERED CASES	AVERAGES	AVERAGES	AVERAGES	AVERAGES	AVERAGES	AVERAGES
No. days illness prior to treatment	7.5	7.2	21.5	8.9	21.7	7.3
No. of stools per day prior to treatment	9.9	14.2	9.8	8.5	9.0	12.8
Age in months	24.7	19.8	10.6	26.1	7.2	19.6
Temperature on admission	100.7	101.5	99.6	101.2	100.8	101.6
Highest temperature	101.7	103.3	102.0	104.0	101.0	103.3
No. days temperatures over 99.8°	3.5	16.0	6.3	11.5	4.3	8.7
No. days in hospital	14.8	22.2	25.4	30.0	13.0	17.2
No. days on straight treatment	6.8	12.9	7.9	11.3	6.5	11.2
No. days on transitional treatment	4.2	14.8	4.8	10.6	4.0	4.0
Total gain in ounces on straight treatment	7.5	1.3	9.3	3.4	16.3	7.2
Total gain on transitional treatment, in oz.	4.5	7.8	6.6	2.8	2.8	4.0
No. calories per pound per day on straight treatment	36.1	33.0	52.4	43.0	49.0	50.3
No. calories per pound per day on transitional treatment	44.8	47.1	57.2	47.0	*	*
No. days stools were liquid	2.3	13.0	6.6	12.4	3.0	7.5
No. days until first soft stools appeared	0.3	0.7	0.9	1.4	1.0	1.4
No. stools per day on straight treatment	3.9	5.2	5.0	5.3	5.9	5.4
Per cent liquid stools on straight treatment	19.4	31.7	36.0	51.5	41.8	33.0
No. stools per day on transitional treatment	3.3	4.1	3.6	2.9	2.1	3.8
Per cent liquid stools on transitional treatment	0	12.2	8.1	21.2	0	8.7
No. days mucus was present	9.0	16.0	6.4	13.8	1.5	7.5
No. days pus was present	3.0	12.4	1.3	5.5	1.0	1.6
No. days blood was present	3.5	12.1	2.3	6.8	0	3.8
Per cent recurrences	16.7	15.4	8.3	0	0	0
Per cent mortality	0	31.6	29.4	53.3	0	11.1

*Diets were so diversified accurate records were not kept.

having bacillary dysentery but from whom the specific organism had not been isolated. Very careful morphologic, cultural, and serologic studies for the identification of suspicious organisms were made. Diagnosis was based on positive bacterial findings in 68.5 per cent of the cases here reported. Although it is realized that any attempt to classify the cases of diarrhea, other than those with positive bacterial findings, is at best a very arbitrary thing, it seemed that the cases which were probably of dysenteric origin but failed to give positive bacterial findings should be included in this report. Therefore, we have designated those cases with history of contact with dysentery, with bloody mucoid stools, with positive proctoscopic findings, and other typical clinical symptoms but failing to give positive bacterial findings as infectious gastroenteritis probably of dysenteric origin.

When it was felt that the improvement in the child's condition warranted a return to the normal formula, the amount of pectin-agar powder was progressively reduced for a few days with the subsequent resumption of the standard feeding routine. The older children were given a transitional diet consisting of two or three feedings of the pectin-agar gel with a modified soft diet fairly high in protein and containing only the bland fruits and very little vegetable material. After a few days, the pectin-agar feedings were discontinued and the regular diet resumed.

RESULTS

Table I gives a summary of the results from the treatment of 52 cases of specific dysentery and 27 cases of infectious gastroenteritis which were probably dysentery. In the various groups soft stools appeared on the average from seven to thirty-four hours after the pectin-agar feedings were first given with an abrupt reduction in the average total number of evacuations daily. In the milder cases the response was often rather spectacular with soft stools appearing within a few hours after the first pectin-agar therapy, but in the more severe and toxic cases, while the appearance of the first soft stools was fairly prompt (twenty-four to seventy-two hours), the general improvement was often slow although steady. Children admitted before the extreme moribund symptoms had developed and treated for at least forty-eight hours showed definite improvement in 73.4 per cent, with reduction in temperatures, improvement in form and contents of the stools, and definite and often very marked decrease in tenesmus and general discomfort.

The average caloric intake per pound ranged from 33 to 52.4 calories and weight gains resulted in each group. The periods of straight treatment averaged from 6.5 to 12.9 days and the transitional diet was given from 4.0 to 14.8 days. The mortality ranged from 0 in gastroenteritis groups of 1936 and 1938 to the high of 53.3 per cent in the bacillary dysentery group of 1937. The mortality for the entire series was 26.6 per cent. The median age of all the patients reported was 10 months.

TABLE II

CASES OF DIARRHEA TREATED WITH THE PECTIN-AGAR FEEDINGS DURING THE LAST THREE SUMMERS

TYPE	1936	1937	1938	TOTAL
Bacillary Dysentery	19	15	18	52
Flexner	18	15	11	44
Shiga	1			1
Sonne			6	6
Hiss-Y			1	1
Infectious Gastroenteritis	6	17	4	27
Parenteral	3	15	16	34
Dietary	1	5	4	10
Miscellaneous		4	3	7
Total of all cases		130		

Table II is the summary of all the cases of diarrhea treated during the three years. Our main interest here is in reporting the infectious type of cases, but we feel it should be mentioned also that in the non-infectious cases this therapy has proved extremely successful.

OBSERVATIONS AND DISCUSSIONS

This report covers a series of unusually severe hospitalized cases of infectious diarrhea. The infants were referred to the hospital from all parts of the state, and often considerable time elapsed between the onset of the symptoms and the time the treatment was started. Patients admitted in comatose state, in whom the moribund course was not altered in spite of all therapeutic efforts and who died within forty-eight hours after admission to the hospital, are not included in this series.

All variations in symptoms were observed, ranging from 7 patients with blood and mucus in their stools, but with little or no fever and giving the appearance of being quite well, to the majority of the cases at the other extreme with marked prostration, high fever, rapid and marked dehydration, extreme emaciation, disturbed consciousness, and, in several cases, death within forty-eight hours after the onset of the diarrhea. Complications were encountered frequently, particularly in the 1937 series. Of the cases of bacillary dysentery and of infectious gastroenteritis treated during the summer of 1937, 81 per cent of the cases had complicating conditions, with otitis media, bronchopneumonia, pertussis, and pyelitis encountered most frequently. When one considers that these infants were not only suffering from the serious gastrointestinal disturbance, but also from one and usually two complications and that the average age for the two groups was 10.6 and 26.1 months, one is not surprised at the mortality rates of 29.4 and 53.3 per cent.

Since the hospital is a state institution for charity cases, the patients came from homes of rather low economic status, and the incidence of malnutrition, even to marasmus with emaciation to almost unbelievable states, was quite high. In those children having poor previous nourishment, the disease was not only severe, but often it developed into a

rather chronic state with frequent complications and necessitating long periods of hospitalization. Ten such cases were encountered in this series with periods of hospitalization ranging from 57 to 87 days.

Of the cases treated, the youngest was 1 month and oldest 7 years, with the age distribution as follows: 1 child of 7 years, 1 of 6 years, 2 of 4 years, 14 between 2 and 3 years, 20 between 1 and 2 years, and the remaining 41 infants being less than 1 year old, with the median age of 10 months for the whole group.

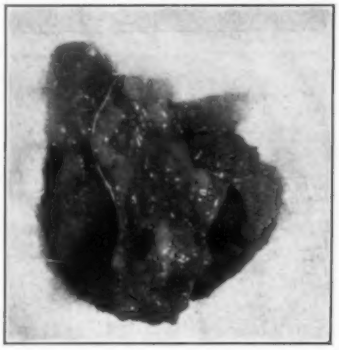

Fig. 1.—Stool resulting from the pectin-agar feedings, showing the peculiar soft consistency.

The stools resulting from this therapy have a peculiar soft consistency (Fig. 1). We wish to emphasize that with this type of diet a great deal of indigestible bulk should be given to make four or more large and bulky stools daily. This is why it seems better in interpreting the response to this therapy, to be guided more by the consistency, whether it is soft or liquid, and the stool contents, whether pus, blood, or mucus is present, rather than by the number or volume of the stools. The prompt appearance of soft stools and the decrease in number of liquid evacuations are of utmost importance in checking the excessive loss of fluids from the already dehydrated infant. In the dysentery cases the stools gave the characteristic foul odor with varying amounts of blood, pus, and mucus. In some stools blood occurred in small streaks, and in others practically nothing but blood and mucus was present. In the stools of the patients fed pectin-agar, the disappearance of the blood, pus, and mucus was measurably more prompt than in the stools of comparable patients treated with other diets, including protein milk, acid milk, and the raw apple.

The rationale of giving a high carbohydrate milk feeding may be questioned by some as it was by us. We have found that the carbohydrate tolerance for our mixture is surprisingly high, and, when it is incorporated in the milk to supply the protein, our patients, in spite of the severity of the disease, have not only maintained their weights

but have shown weight gains. In our original study no milk was used; however experience has taught us that high concentrations are equally well tolerated even in severe specific dysenteries. Special feedings devised for a few extremely marasmic infants incorporating powdered milk, egg yolk, and vitamin concentrates to give caloric values as high as 100 calories per pound have been used successfully and apparently have saved the lives of some who were getting progressively worse on other diets.

The addition of the pectin-agar powder to the fresh milk brings about a precipitation of the milk in an extremely fine grained curd, which probably tends to increase the digestibility of the milk. This reaction was described by Joseph[16] as apparently due to some specific property of the colloidally dispersed pectin, either from a process of sensitization or through the removal of calcium from the caseinate complex by the pectin, by adsorption or actual chemical combination. A similar reaction has been observed when apple powder is added to milk.[17]

During the 1936 series recurrences of the symptoms during or shortly after the patients had been given the transition diet were encountered in 16.7 to 15.4 per cent of the cases. However, during the 1937 and 1938 series, the recurrences were very rare. We have come to realize that in states of intestinal disturbances, such as encountered in these severely ill infants, the treatment is not a matter of two or three days but of a week or more. Our return to the normal regime has been postponed until the child was definitely improved, and then a more gradual transition is used.

In this series of 79 cases, only 5 infants were encountered who because of excessive vomiting, extreme distention, or failure to respond to the pectin-agar therapy as well as expected were changed to other types of feedings. Three of these patients showed improvement on the changed feedings, and of the other two, one continued to vomit all feedings and the other showed no change in degree of distention before death.

The response to this type of feeding is measurably more prompt and complete than that observed in similar cases treated by other dietary means. The results from feeding the apple diet to a group of infants and children suffering from various types of diarrhea were compared with the results from a similar group given the pectin-agar feedings.[1] It was found that when the raw scraped apple was fed, longer periods of treatment and transition were required; recurrences were more frequent; the appearance of soft stools, the cessation of liquid evacuations, and the disappearance of blood, pus, and mucus were not as prompt as in the group fed pectin-agar; the feedings were not as well taken, and there was a weight loss, as compared with a gain in weight observed in the pectin-agar group. Again in a comparison of the results from the use of lactic acid milk and pectin-agar in treatment of cases of bacillary dysentery,[18] it was found that patients responded more quickly to the pectin-agar feedings and required a shorter period of treatment, that 41 per cent

liquid stools occurred with the lactic acid milk as compared with 28 per cent with the pectin-agar, and that liquid stools persisted in the lactic acid group for 16.2 days as compared with 8.9 days in the pectin-agar group.

Speculation as to the mode of action of the pectin and of the agar in the treatment of diarrheas has been rather widespread during the last few years. Scheer[19] used agar milk combinations for diarrhea and suggested that the agar acts as a colloidal disperser of the milk protein, aiding in the ease of digestion, acts on the acid base balance, and aids in controlling the water balance. These ideas were also endorsed by Calvo.[20] Frias[21] considered the action more on the motility of the gastrointestinal tract with a regulating action neither laxative nor astringent. Little can be added to the summary of Manville and collaborators[22] on the various actions of pectin. They considered as important factors pectin's great absorptive capacity for bacteria and toxins, its ability to take up large quantities of fluids and thus provide bulk in the intestines, the buffer action, the action as a protective colloid, and the detoxifying action of the galacturonic acid formed by the breakdown of the pectin.

Since the bactericidal action of pectin has been demonstrated to be specific for a metal pectin product[23] and not a property of pectin per se, it does not seem probable that this bactericidal action has any therapeutic effect in the gastrointestinal tract. Work which was completed recently in this laboratory showing that in dogs pectin has a prophylactic as well as curative action for experimental ulcers resulting from administration of cinchophen[24] seems to offer more evidence to justify the use of this therapy. The action of the pectin in this work was felt to be, in part at least, a mucus-sparing or a protein-sparing action probably due to the uronic acid content of the pectin, which acted in a manner similar to that of glucuronic acid.

The total action of this pectin-agar combination is not completely understood, but it would seem to be a combination of the physicochemical and mechanical actions of the materials. Since the agar and pectin make a gel which passes through the gastrointestinal tract as such, liquid stools, in most instances, are a physical impossibility. The formation of the gelatinous mass and the breakdown of the pectin with the liberation of galacturonic acid, the absorbing, emulsifying, detoxifying, and diverse other actions of pectin and its split products result in a cooperative action to give the total therapeutic effect.

The use of this high caloric therapy for diarrhea fits in with the modern method of treating typhoid fever since both feed the patient rather than starve him and strive to maintain as good nutritional state as possible. It seems that this pectin-agar therapy is particularly suitable for treatment of these severe infectious diarrheas since it not only has a therapeutic action on the diarrheal symptoms, but also offers a well-balanced, nourishing, and easily digested food which tends to keep up the infant's resistance until the time when the natural immunity can

be developed. This diet has proved very practical and workable in that its method of preparation is simple; the average child takes the feedings quite readily; and it is made from the stable standard powder which is not subject to seasonal supply.

SUMMARY

A series of 52 cases of bacillary dysentery and 27 cases of infectious gastroenteritis, probably dysentery, in infants and children treated with the pectin-agar dextrimaltose combination is reported.

There was a definite and quick response with soft stools within an average of thirty-four hours and a gradual and steady improvement in 73.4 per cent of the cases.

The calorie intake averaged from 33 to 52.4 calories per pound per day, and average weight gains were observed in every group.

The mode of action of this therapy is probably both physicochemical and mechanical, with the uronic acids playing an important part.

The diet is peculiarly suitable for infectious cases, since besides having a definite therapeutic action, it is high in calories, well balanced, and easily assimilated, and it maintains nutrition while the body has a chance to develop the necessary immunity. It is easily prepared, very readily taken, available, standardized, and safe. Our experience continues to confirm our early observations that this pectin-agar diet very definitely more quickly and completely produces formed stools with fewer recurrences than other accepted methods, including the apple diet.

The authors wish to acknowledge the suggestions and assistance of L. T. Meiks, M.D., and Edith Haynes, Ph.D., in this study.

REFERENCES

1. Winters, M., and Tompkins, C. A.: Am. J. Dis. Child. **52**: 259, 1936.
2. Moro, E.: Klin. Wchnschr. **8**: 2414, 1929.
3. Wolff, S.: Deutsche med. Wchnschr. **56**: 2211, 1930.
4. Schreiber, W.: Med. Klin. **27**: 1452, 1931.
5. Mouzon, J.: Presse méd. **40**: 1004, 1932.
6. Heisler, A.: Therap. d. Gegenw. **74**: 488, 1933.
7. Malmberg, N.: Svenska läk.-tidning. **31**: 382, 1934.
8. Earnshaw, P. A.: M. J. Australia **2**: 305, 1934.
9. Hartwich, A.: München. med. Wchnschr. **80**: 1217, 1933.
10. Schlesinger, B.: Proc. Brit. Pediat. A., Arch. Dis. Child. **11**: 169, 1936.
11. Skinner, H. H.: Northwest Med. **35**: 313, 1936.
12. Sabri, I. A., Abboud, M. A., and Ali, M.: Arch. Dis. Child. **12**: 225, 1937.
13. Smith, E. E., and Fried, R. I.: J. PEDIAT. **10**: 495, 1937.
14. Malyoth, G.: Klin. Wchnschr. **10**: 1159, 1931; **13**: 51, 1934.
15. Baumann, T., and Forschner-Boke, H.: Ztschr. f. Kinderh. **56**: 514, 1934. Baumann, T.: Monatschr. f. Kinderh. **60**: 81, 1934.
16. Joseph, G. H.: J. Soc. Chem. Industry, March 21, 1930.
17. Reithel, F. J., and Manville, I. A.: Am. J. Dis. Child. **56**: 235, 1938.
18. Washburn, G.: J. Am. Diet. A. **14**: 34, 1938.
19. Scheer, K.: Med. Welt **10**: 21, 1936.
20. Calvo, M. A.: Siglo méd. **97**: 290, 1936.
21. Frias, B.: Arch. de med., cir. y especialid. **38**: 798, 1935.
22. Manville, I. A., Bradway, E. M., and McMinis, A. S.: Canad. M. A. J. **36**: 252, 1937.
Manville, I. A.: Arch. Ped. **55**: 76, 1938.
23. Haynes, E., Tompkins, C. A., Crook, G. W., and Winters, M.: Proc. Soc. Exper. Biol. & Med. **39**: 478, 1938.
24. Winters, M., Peters, G. A., and Crook, G. W.: Am. J. Digest. Dis. & Nutrition. **6**: 12, 1939.

CONGENITAL CARCINOMA OF THE THYMUS WITH EXTENSIVE GENERALIZED METASTASES

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PRIMARY carcinoma of the thymus is not a common finding and still less common is congenital primary carcinoma of the thymus. The literature on the subject is summarized in an extensive review by Crosby,[1] who reports 44 cases of carcinoma collected from the literature up to 1932. In 1936 Slesinger[2] brought the total number, including one case of his own, to 53. Additional cases have been reported by McDonald,[3] Decker,[4] Kahr,[5] and Goyle, Vasudevan and Krishnaswamy.[6]

The majority of these reports are those of adults who presented the typical findings of tumor of the thymus upon clinical examination. Bedford[7] described the only case that involved a newborn infant, a child who lived 17 days. There was a generalized eruption on the skin of moderate degree clinically suggestive of syphilis. The blood Wassermann, however, was negative on two occasions. A history of repeated attacks of dyspnea, together with physical and x-ray examination of the chest, made possible a diagnosis of enlarged thymus. At autopsy a large thymic carcinoma was found. The tumor was firmly adherent to the lungs, and microscopic examination revealed numerous metastases to the lungs, liver, bone, and skin.

The present case, observed at Mount Sinai Hospital, Cleveland, is similar in many respects to that of Bedford; the extent of the metastases, however, is much greater. Both presented essentially the same clinical pictures in newborn infants, and syphilis was suspected and looked for in each. In both, at autopsy a highly malignant carcinoma of the thymus was found, together with extensive metastases to other organs.

CASE REPORT

The mother was a 29-year-old primipara, who was admitted in active labor. She gave a history of congenital syphilis, with an undetermined amount of treatment administered at various times. Her slide test for syphilis at the time of delivery was two-plus diagnostic and four-plus exclusion. The only other point of interest was the habitual use of large amounts of a phenolphthalein laxative.

Shortly after admission she gave birth to a full term male child weighing 2,860 gm. The delivery was normal and unattended by any appreciable difficulties. A striking generalized eruption involving all portions of the skin of the child was noted immediately (Fig. 1). The lesions were variable in appearance; some were merely small ecchymotic flecks, while others were macular, papular, vesicular, or even pustular. A few of the more prominent lesions appeared hemorrhagic. The lesions varied from 1 to 8 mm. in diameter. On several occasions the temperature

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rose to 100° F., but no marked elevation was noted at any time. There was a steady loss of weight with death occurring after seven days, apparently due to increasing respiratory distress. During this period, the skin lesions changed somewhat; many steadily enlarging, breaking down, and becoming crusted over, while at the same time other new ones appeared.

Fig. 1.—Photograph showing generalized eruption noted at birth. Macular, papular and vesicular lesions present everywhere varying from 1 to 8 mm. in diameter.

The *laboratory reports* of interest were as follows:

Slide test for syphilis on umbilical cord blood and on baby's blood was negative in both the diagnostic and exclusion tests.

Blood counts showed red blood cells, 4,740,000; white blood cells, 18,500; with the following differential count: mature polymorphonuclear neutrophiles, 37 per cent; juvenile cells, 26 per cent; metamyelocytes, 10 per cent; myelocytes, 5 per cent; myeloblasts, 1 per cent; eosinophiles, 3 per cent; monocytes, 2 per cent; and lymphocytes, 16 per cent.

Bleeding time was ½ minute; clotting time, 3 minutes; and the icterus index, 31.

Numerous smears of the skin lesions stained by the Fontana method showed no spirochetes. Gram stains of skin lesions demonstrated occasional gram-positive cocci. There was also a slight growth of *Staphylococcus aureus* upon culture of material from a lesion.

The various clinical impressions were recorded as follows: Third generation syphilis; phenolphthalein rash (due to excessive use by the mother); a blood dyscrasia; and a widespread metastasizing tumor such as a Kaposi sarcoma. However, no satisfactory final diagnosis was made clinically.

Autopsy

Skin.—There is a generalized eruption with innumerable rounded and irregularly shaped lesions, varying in size from 1 mm. to 8 mm. in diameter. These lesions are extremely variable in appearance, ranging from single small intracutaneous flecks, to large vesicular, pustular or crusted areas. Some sites contain grayish or reddish brown fluid material. The lesions are numerous and most striking on the soles of the feet.

Mouth.—Mucous membranes show a number of small, apparently ulcerating lesions similar to those in the skin.

Heart.—The only appreciable gross abnormality is a small rounded reddish subepicardial area which is at the base of the right ventricle and extends into the underlying myocardium.

Lungs present a striking picture. They are larger and firmer than average. Many bleblike areas, variable in size and discolored gray and deep red, are seen through the pleura and on section of parenchyma. In numerous places there are apparently necrotic areas with umbilication or actual defect formation. The entire pulmonary tissue presents a deeply congested, mottled, and dark red appearance.

Pancreas is of average size and shows numerous well-defined grayish white areas of fine architecture, suggesting granulomas or tumor tissue.

Thymus is moderately enlarged. There is no recognizable thymic structure. Tissue is firm and on section is gray with numerous areas that suggest necrosis or suppuration. Small granuloma-like nodules are noted in places. Regional structures are not adherent to the thymus, and there is no apparent extension of the abnormal thymic tissue to lungs or mediastinal structures.

Mesenteric Lymph Nodes.—Several slightly enlarged, round, discrete, grayish fleshy nodes are present.

The remaining organs, including brain, pituitary, and pineal gland, show no gross lesions.

Microscopic Description

Microscopic examination of the various tissues shows involvement of epicardium, lung, liver, spleen, pancreas, large intestine, thymus, lymph nodes, brain, skin, and bone marrow. The lesions are essentially of two types.

The first type, seen in the epicardium, liver, spleen and bone marrow, suggests an infiltrative or possibly a granulomatous process rather than a tumor. The involved tissue in these organs appears to be made up of large irregularly shaped cells, in loosely bound arrangement. Nuclei are rounded and vesicular and show an occasional chromatin knot. Cytoplasm is pale staining. Rare mitotic figures are

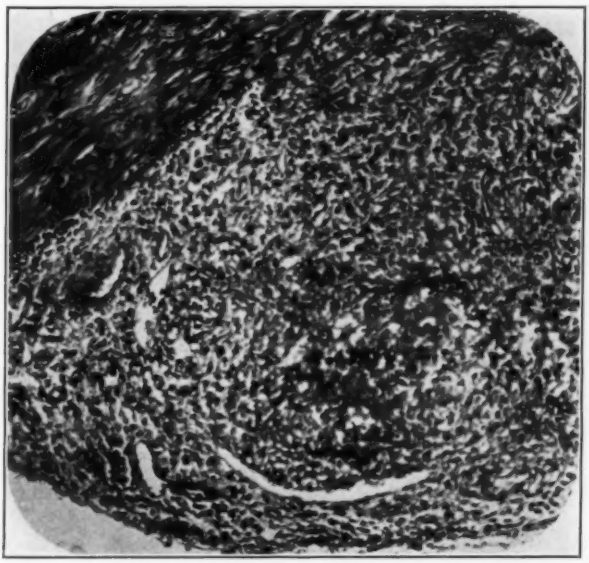

Fig. 2.—Photomicrograph of epicardium. Metastasis showing a granulomatous appearance with a small area of central hemorrhage.

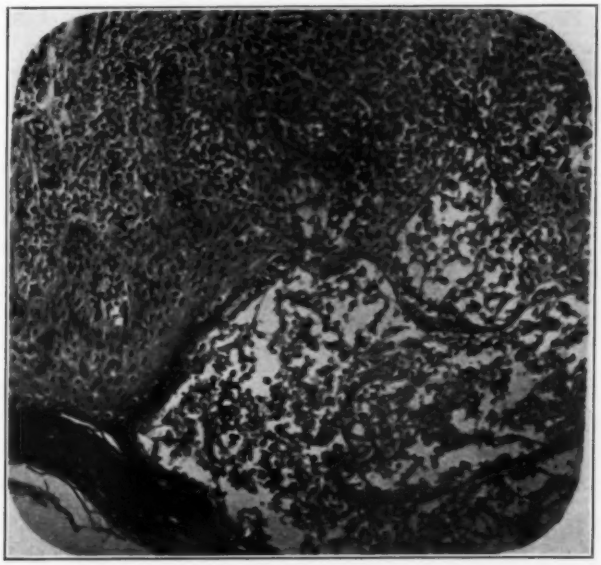

Fig. 3.—Photomicrograph of skin. Metastatic area with necrosis of tumor and ulceration of epithelium.

noted. There is no evidence of tissue destruction although occasional small areas of hemorrhage are present. The involved epicardium (Fig. 2) shows such a typical lesion.

In the skin the lesions in many areas are more advanced and suggest metastases with necrosis. Here poorly circumscribed rounded nodules are found made up of cells similar in structural and histologic arrangement to that described above. The cells in places extend as small strands into the underlying tissues. The epithelium immediately overlying the nodule frequently appears ulcerated and necrotic (Fig. 3).

The second type of lesion, which definitely suggests tumor, is found in the other involved organs. In the lung, for instance, the greater portion of the tissue is made up of a diffuse sheetlike mass of cells in which the usual lung markings may still be made out. In many areas there is a suggestion of an alveolar arrangement. The cells show a large rounded nucleus and a moderate amount of pale stained cytoplasm. Many cells are polyhedral. In some areas numerous small dilated and engorged blood vessels are present, apparently forming a part of the tumor. Occasional large multinucleated giant cells are present (Fig. 4). In places there is a suggestion of tumor cells within vessel lumina.

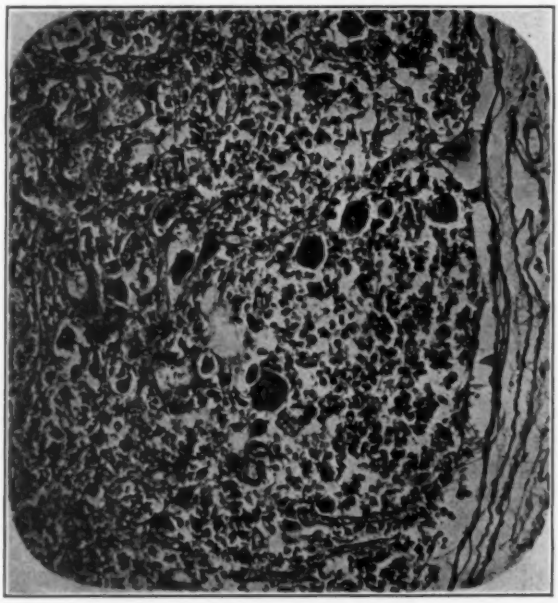

Fig. 4.—Photomicrograph of lung. Metastasis showing abundant giant cells.

The tumor is apparently oldest and furthest advanced in the thymus. The section here shows no recognizable thymic structures. There are numerous small roughly rounded areas in which the tissue appears necrotic. There are also deeply blue stained sites suggesting calcification (Fig. 5). An occasional giant cell is noted regional to the necrotic and the calcified areas. The greater portion of the section is made up of a sheet of tumor tissue with architecture in places vaguely alveolar in appearance. Cells are large, polyhedral and rounded with prominent, rounded, poorly stained nuclei. The cytoplasm is variable in amounts. In places it is abundant, lightly stained and vesicular, whereas in other places there is very

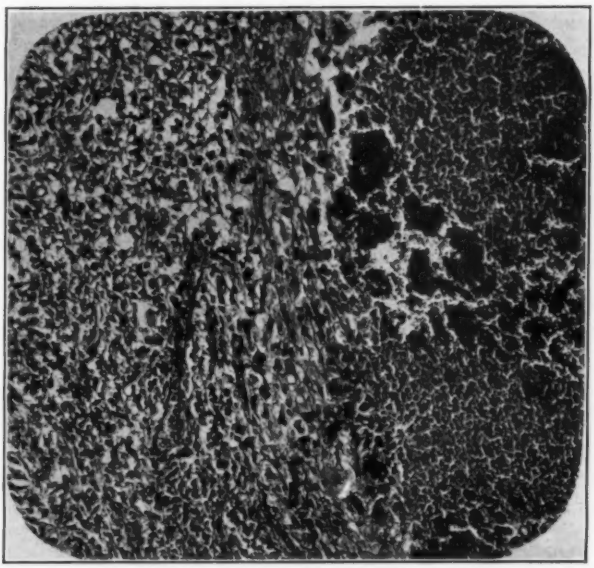

Fig. 5.—Photomicrograph of thymus. Primary tumor showing the diffuse sheet of pleomorphic tumor cells and the regional area of necrosis and calcification.

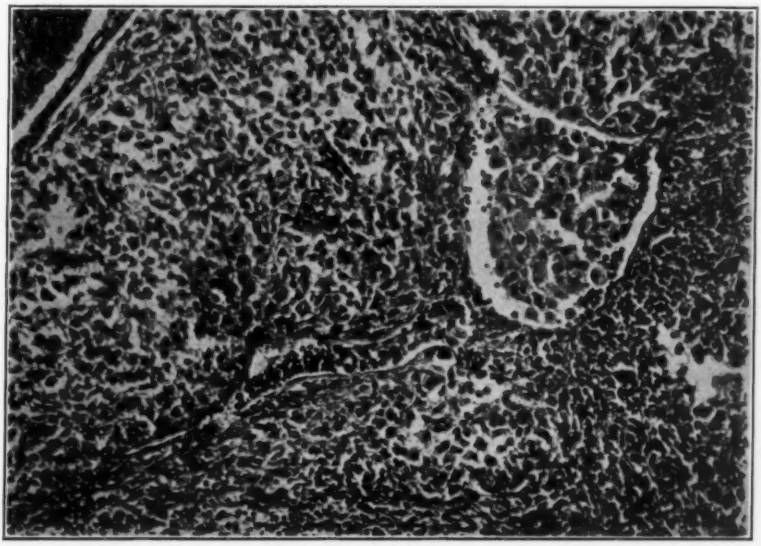

Fig. 6.—Photomicrograph of thymus. Primary tumor with tumor cells invading and distending lymphatic spaces.

little present. Mitosis is noted occasionally. There are areas where the cells appear compact and other sites where the cellular structure is loosely arranged with irregular spaces between the cells. The tumor is separated into poorly defined nodules by septumlike structures made up of spindle cells. Tumor tissue in places apparently fills lymphatic spaces (Fig. 6). At the periphery there are small focal nests of round cells present.

Similar lesions are noted in the pancreas, lymph nodes and liver.

Because of the pleomorphic appearance of the tumor the slides were submitted to Dr. James Ewing, and his comments are as follows: "The structure reminds me strongly of the large cells of thymoma, and this, I think, is the best interpretation. The giant cells recall some of the endotheliomas of lymph nodes which I used to describe. . . . My guess would be thymic carcinoma with metastases in an infant."[8]

COMMENT

The clinical diagnosis of thymic carcinoma is obviously difficult. The most prominent clinical symptoms in the adult are respiratory and circulatory disturbances due to pressure. Hence, dyspnea and cyanosis are the most striking features of the disease. In the newborn infant, however, dyspnea and cyanosis are usually attributed to other more common causes such as cerebral injury, atelectasis, or congenital heart disease. Supracardiac dullness, which is one of the cardinal signs of this condition in the adult, is not a dependable finding in the newborn.

The extensive congenital lesions of the skin in the case reported here should make one realize that he is dealing with a generalized pathologic process which has also invaded the skin. Once syphilis has been ruled out, one should think of the possibility of metastatic malignancy. Thorough physical and laboratory examinations, including x-rays of the chest and long bones, should be done in the search for the primary lesion.

SUMMARY

The second case of congenital primary carcinoma of the thymus with extensive metastases to be recorded in the literature is reported above.

REFERENCES

1. Crosby, E. H.: Am. J. Cancer **16**: 461, 1932.
2. Slesinger, H. A.: J. Lab. & Clin. Med. **22**: 151, 1936.
3. McDonald, S.: J. Path. & Bact. **35**: 1, 1932.
4. Decker, H. R.: J. Thoracic Surg. **4**: 445, 1935.
5. Kahr, H.: Zentralbl. f. Gynäk. **60**: 1751, 1936.
6. Goyle, A. N., Vasudevan, A., Krishnaswamy, K. G.: Indian J. M. Res. **24**: 153, 1936.
7. Bedford, G. V.: Canad. M. A. J. **23**: 197, 1930.
8. Ewing, J.: Personal communication.

SUBCUTANEOUS EMPHYSEMA IN THE NEWBORN INFANT

Case Report

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RECENTLY we encountered a most unusual condition in a newborn infant, the rarity of which warrants its reporting.

J. D., the second of twins, was born on April 7, 1938.

H. D., gravida ii, aged 25 years, the mother, was delivered of a stillborn child in 1936. The presentation at that time was a footling breech. The cause of death of the infant was not known.

The last menstrual period of the mother was June 30, 1937, making the expected date of delivery April 14, 1938. Pregnancy progressed normally the first months although the fundus height did seem too great for the period of gestation. On Jan. 7, 1938, an attempt was made without success to diagnose twins. We tried to rotate the breech that was presenting but desisted because of the vertigo which came on immediately. On January 25 the suspicion of twins was confirmed by examination by x-ray. At this time the urine had present a faint trace of albumin. On March 22 the blood pressure was 154/86, weight 166 pounds, height of the fundus 39 cm. The urine showed a marked trace of albumin. Since the patient was so miserable that it was pitiable, an attempt was made to induce labor by medical means on March 30. This was not successful.

Labor began on April 6 with a breech presenting. The membranes ruptured spontaneously about three hours after the onset. The first stage lasted approximately 10 hours. During this time pentobarbital (nembutal) gr. 6, and hyoscine gr. 1/100 were given in divided doses. Rectal ether was administered, but very little of it was retained. During part of the second stage, which lasted between forty-five minutes and one hour, gas and oxygen were given with contractions.

Under ether anesthesia the breech was delivered spontaneously. Some assistance was given in the delivering of the shoulders and head. Eleven minutes later the second amniotic sac was ruptured, and the second infant delivered by version and breech extraction. The placenta was delivered by Brandt's maneuver six minutes later.

The first baby, a girl, breathed immediately and cried lustily at birth. The second infant, a boy, made strenuous gasping attempts to breathe. At first he was pink, but soon became cyanotic. While he was attempting to breathe, the intercostal spaces drew in with great force. The fauces and trachea were cleared with a rubber catheter. In a short time it was noticed that the left side of the chest and the left supraclavicular space and neck up to the chin were markedly swollen. The mass in the neck was about the size of half an orange. Crepitation was felt in these areas. Oxygen was administered continuously. Breath sounds were heard over the right chest, but none on the left. A radiogram taken at six hours showed a completely atelectatic left lung.

The baby cried fifty minutes after delivery. Coramin 0.5 c.c. and 10 c.c. of his mother's blood (the latter is a routine procedure) had been given intramuscularly. Oxygen was continued for eighteen hours because, on discontinuing it, cyanosis was noticed. The emphysema was still present, more noticeable if anything. At thirty hours, examination by x-ray showed the left lung clear again.

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The emphysema slowly diminished in extent and had disappeared by the fifth day. Except for a slight feeding problem, his progress has been normal. The girl, who weighed 5 pounds 14 ounces at birth, weighed 16¾ pounds on Jan. 6, 1939; the boy, who weighed 5 pounds 11 ounces at birth, weighed 18¼ pounds on the same date. Incidentally, they won a prize at the county fair.

COMMENT

Subcutaneous emphysema is "one of the rarities of medicine from intrinsic causes."[1] The cause in this case, we think, was the violent gasping attempts of the baby to breathe after birth. We think the extremely vigorous attempt to breathe ruptured one of the alveoli, allowing air to escape. The air must have filtered into the mediastinum to have been noticeable in the neck. The attempted external version could hardly have caused the condition, because the time element would make us think a permanent defect would have resulted and a larger area of the lung would probably have been affected. The version and breech extraction were accomplished with no difficulty or trauma. It is possible to cause such a condition by injudiciously inflating the lung mechanically. Such was not the case here, as the emphysema was noticed before oxygen therapy was given.

Slot and Brown[2] have recently reported a case similar to ours and have reviewed the literature. Treatment is the administration of oxygen until the condition rights itself. Puncture of the emphysematous area is not advised because of the danger of infection. It might be possible, however, that in a premature infant the accumulation of air in the neck might suffocate the child because of pressure on the trachea.

REFERENCES

1. Faber, N. K.: Am. J. Dis. Child. **19**: 388, 1920.
2. Slot, G., and Brown, W. D.: Brit. J. Child. Dis. **35**: 116, 1938.

A BUCCAL OXYGEN-ETHER CATHETER

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WHETHER in the home or at the hospital, at some time or other the physician will encounter the problem of giving oxygen, oxygen-carbon dioxide, or oxygen-helium. I wish to present a method of giving these gases which gives the greatest comfort to the patient with the least interference. It is to do away with factors which hinder the normal usages of the nasal passages.

The average physician does not use an oxygen tent readily because of its bulk, transportation problems, and perhaps because of the financial factors. The mask and bag method for the administration of oxygen limits the use of the nose and mouth. An oxygen room would be the ideal thing, but it is impracticable. The use of tanks from which oxygen is made to bubble through water in a wide-mouth stoppered bottle is one of the most popular methods in use today.

On the market today are a variety of metallic tubes to aid in carrying this oxygen to serve the patient. You may encounter in the current surgical supply catalogues the Bullowa nasal tube, the Connel nasal tube, the single nasal tube of Gates, the Gwathmey nasal tube, and the Sanford nasal tubes. In addition small rubber catheters, which are also inserted intranasally, are used in many hospitals.

My criticism of the catheter is that it obstructs the nasal passages. In pneumonia we should have all the respiratory channels free for their physiologic purposes. The rubber catheter gags some patients easily. The types that plug both nares interfere with mucous discharge. The objections to the mask type are that it causes apprehension, does not allow room for sipping fluids or foods, and hinders the patient in calling readily if he needs assistance.

To overcome these criticisms I have devised the buccal catheter. By means of it oxygen is conveyed via the oropharynx to the lungs and leaves the nasal passages free.

This instrument is constructed so as to lie adjacent to the buccal mucous membrane and lateral to the dentogingival area. Only the inner aspect of the instrument, which is the side facing the oral cavity, permits the oxygen to escape. The patient can cry out if he desires and can sip fluids without disrupting the mechanism. Thus it helps satisfy oxygen want, allows the physiologic action of the nasal and pharyngeal passages, keeps the patient as comfortable as humanly possible, and perhaps with less apprehension.

The principle of the buccal catheter and its construction are simple and economical. Two brass tubings 1/16 inch in diameter and 4¾ inches long are so shaped as to be pyriform at one end, the end that is in the oral cavity. Then the portion of the tubing at the lower lip level is bent in an angle of about 110 degrees with the chin base. One inch of tubing is allowed for resting on the chin base under two hooklets from which it may pivot. The final ⅛ inch of tubing is bent at right angles to the chin base portion. To this portion rubber tubing is attached to lead to the oxygen. The other end of the tubing is closed. The chin rest has two hooklets on each side, 1¼ inches apart. These hooklets are raised portions of the zinc or galvanized tin ½ inch from each other. The chin base is molded to fit the natural curvature of the chin. Five perforations are drilled into the tubing of each pyriform wing on the side that faces the teeth only.

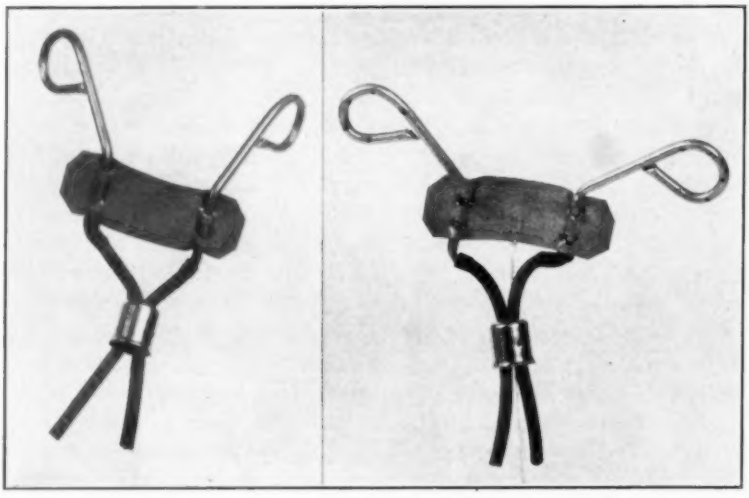

Fig. 1. Fig. 2.

Fig. 1.—Front view. The ring about the tubing adjusts the abduction of the wings.
Fig. 2.—Rear view. This shows the perforations on the pyriform wings which face each other.

To use, raise the lips and slip the pyriform wings between the teeth and the buccal mucous membrane. To adjust for the different widths of mouths encountered slide a ring about both tubings which lead from the arms of a Y glass tube to the buccal catheter. This causes the wings of the catheter to abduct and have more firmness against the cheeks since the right angle portions turn inward. If too firm, the slipping of the ring downward releases the pressure proportionally. Adhesive tape is applied to the ends of the chin base for security

against the skin. However when in the recumbent position it has a tendency to stay in place because of the pressure against the buccal mucous membrane.

This buccal catheter serves another very useful purpose in oral surgery—the giving of ether. In doing tonsil or adenoid operations, the ether hook of the suction and pressure pump can be removed and replaced by attaching it to the buccal catheter. It remains out of the way of a mouth gag very nicely. Thus this catheter serves a dual duty.

The illustrations show the simplicity of this apparatus.

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THE FUTURE OF AMERICAN PEDIATRICS

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PEDIATRICS is one of the oldest, if not the oldest, of the specialties; its foundations were laid during the Renaissance (1453-1600) by Bagellardus, Metlinger, Phaer, Hieronymous, Sainte Marthe, Glisson, and others.[1] By the twentieth century the pediatrists were recognized as specialists to whom general practitioners referred patients for diagnostic and therapeutic advice, similar to the practice in other specialties. During the present generation, the amount of teaching of children's diseases in the medical schools and the number of pediatric internships in the hospitals have grown tremendously. As a result, the number of pediatrists in the United States rapidly expanded to the present total of 3,383. The specialty soon lost its consultative function and became general practice with an age limit of puberty.[2] During the last decade the introduction of preventive measures, many of them developed by pediatrists, has completed the metamorphosis, so that pediatrics today is more of a division of public health and preventive medicine than a clinical specialty.

This change in pediatrics has been recognized by the federal government, and the Technical Committee on Medical Care of the Interdepartmental Committee to Coordinate Health and Welfare Activities on July 18, 1938, recommended to the National Health Conference[3] the annual expenditure of $225,000,000 by the tenth year of the program, to reduce infant and maternal morbidity and mortality.* Part of this plan already

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*_Abstract From the Recommendations of the Technical Committee on Medical Care_[3]

"Expansion of the program for maternity care and medical care of children, including health supervision of pregnant women and of infants and preschool children by local physicians, public health nursing services, health supervision of school children, and the services of dentists, nutritionists, health educators and medical social workers. Medical care of mothers and their newborn infants, throughout the period of maternity and the neonatal period, including care of the mothers at delivery in the home or in hospital, and of their newborn infants, by qualified local physicians with the aid of specialized consultants, assisted by nurses, preferably public health nurses, trained in obstetric nursing procedure. Facilities for expert diagnosis and care in diagnostic or consultation centers and in the home. Hospital care as necessary for medical, social, or economic reasons. Health supervision, medical care, and, when necessary, hospitalization of older infants and children—the health supervision and medical care to be provided by qualified local physicians with the aid of specialized consultants in local consultation or diagnostic centers, or elsewhere when the ill child cannot be brought to the center.

"To provide for such an expanding program, an annual cost to federal, state, and local governments of $95,000,000 is estimated for maternity care and care of newborn infants, based on the needs of families on relief or with incomes of less than $1,000 a year (approximately 1,100,000 live births and stillbirths annually), including cost of medical, nursing, and hospital care; development and maintenance of 10,000 additional maternal and child health consultation centers to serve smaller cities, towns and rural areas; development of centers for postgraduate education of physicians, nurses, medical social workers; and federal and state administration. For health supervision and medical care of children, the average unit cost of providing a minimum of essential medical services is estimated to be $10 per child per year, or an additional annual sum of $130,000,000 for the 13,000,000 children under 15 years of age in the third of the population in need of financial assistance in obtaining basic health and medical services."[3]

is in effect, i.e., federal and state funds in 1938-39 paid for 50 directors of state bureaus of maternal and child health, 30 of whom have been trained in pediatrics, 28 full-time pediatrists, 13 full-time obstetricians, 2,713 prenatal clinics or conferences, and 6,033 child health conferences, in addition to the personnel of the U. S. Children's Bureau.[4] The scope and content of the present program are described below.*

Although everyone realizes that additional infant and maternal health services should and must be made available to the public, especially those in the lowest economic group, it must not be forgotten that poverty is not the sole reason for failure to obtain adequate medical service. The fact that the lowest economic group of the public receives less medical care and has more illness[3] often may be due to ignorance of the necessity for adequate medical care and of the availability of the present medical facilities. For example, the fact that 19 per cent of the pediatric deaths in 1937 in one state occurred in children who were not taken to their physicians is not prima facie evidence that this absence of medical care was due to poverty and the lack of medical resources. Inadequate pediatric care in many instances is due to the ignorance of the public in availing themselves of the facilities already available, rather than to the lack of medical or economic resources. As illustrations, among the ten diphtheritic patients treated at Duke Hospital during the past month,

*"From the plans submitted by the several states, it becomes apparent that the functions of the state divisions of maternal and child health are as follows: (1) To seek the cooperation of the physicians of the state in extending statewide facilities for continuous health supervision throughout pregnancy, infancy, and childhood, and in providing care for sick children and for women at delivery; (2) to seek the cooperation of physicians and all other citizens of the state in informing the public as to what is good maternity care, infant care, and care of children at different stages of growth and development, and how facilities for such care may be made available in each locality of the state; (3) to develop maternity and child health services in all parts of the state through local health units; (4) to aid in the organization of local health units through the provision of child health or maternity services in areas not yet fully organized; (5) to be responsible for the establishing of high standards of service in the maternal and child health field; (6) to cooperate with all other bureaus of the state health agency in activities affecting the health and welfare of children and mothers, such as public health nursing, control of communicable diseases, including tuberculosis and syphilis, collection and study of vital statistics, control of the milk and water supply; (7) to cooperate with other state agencies concerned with problems of child health or welfare, as the bureaus of child welfare, departments of education and the agriculture extension service of the departments of agriculture; (8) to cooperate with medical and other professional groups in providing facilities for post-graduate education in maternity care and care of children and the related fields of nutrition and dental care, and (9) to promote health education through the schools and the general public.

"The maternal and child health services that are carried out under state plans are basically those commonly described as health supervision: (1) Prenatal clinics and child health conferences conducted by physicians with the aid of public health nurses; (2) home visiting by public health nurses for teaching maternal, infant, and child hygiene, and for instruction in bedside nursing care, and (3) nurses' classes or conferences with mothers for educational or follow-up purposes.

"No specific definition of 'crippled child' was given in the wording of the Social Security Act, although several definitions had been proposed in the hearings before Congress. An investigation of the laws under which state agencies were operating showed variations extending from a very strict definition limiting the services to children with motor disabilities to a very broad definition and interpretation, which included all physically handicapped children who could be benefited by medical or surgical treatment. The various definitions of a crippled child incorporated in the laws of the several states have been accepted, for the present, with the idea that in actual practice definitions will be broadened gradually to include as wide a range of crippling conditions as is practicable within the limitations of the available funds. A few states have included such conditions as rheumatic heart disease and diabetes, but most of the cases accepted for care have been orthopedic and plastic conditions. As the peak load of children awaiting orthopedic care when the Social Security Act became effective is passed, it is possible that proportionately more care may be given to children crippled from cardiac conditions, especially in those states where rheumatic disease is common. Children whose chief disability is incurable blindness, deafness, or mental defect, and those having abnormalities requiring permanent custodial care are considered beyond the scope of this program."[5]

eight were not taken to their physicians for an average of five days after the onset, and, of nine other children suffering from diphtheritic paralysis, seven were not taken to physicians until the onset of paralysis.[5] The parents had not realized the possibility that a "sore throat" might be diphtheria. Yet diphtheria antitoxin is supplied at cost by the state laboratory and is given free in many counties. Although free toxoid is supplied and its usage is urged by health departments, many parents fail to appreciate its value.* In Durham County, which is typical of most American counties, the medical profession, the infant feeding clinics, the health department, the county physician, and the Watts, Lincoln, and Duke Hospital Clinics can provide the necessary preventive and therapeutic measures, regardless of the poverty of the patient, if the public is made aware of their necessity. The Durham-Orange County Medical Society recently has authorized a series of unsigned newspaper articles on preventive pediatrics, calling attention to the unnecessary deaths, and the means of preventing them. Syndicated medical articles have made remarkable progress in educating the public, but as yet they do not reach those who do not read the newspapers.

National, state, county and city advertising campaigns in newspapers, buses, billboards, and radio, and through churches, schools, the Parent-Teachers' Association, the American Legion, etc., on the necessity for antenatal, natal and postnatal care and the medical facilities available, conducted by publicity experts, are necessary to reach more of the population. If, through advertising, a public demand can be created for automobiles, electric iceboxes, certain brands of cigarettes, and patent and home medicines (which represent 14 per cent of the present medical costs[6]), cannot the people be taught to seek adequate medical service? Better pediatric and obstetric care and a lower infant and maternal mortality can be obtained by a smaller amount of money spent in teaching the public to utilize the present medical facilities than would be required for providing additional medical resources. After an educational program has produced a demand for more medical care, the medical services can be extended as they are needed. The public gets the product it demands, whether it is medical care or a nationally advertised variety of tooth paste. The American Academy of Pediatrics shortly will start such a pediatric publicity campaign.

Increased education of the public, in addition to increasing the amount of medical service requested, will raise the standard of that service. If a public demand for preventive pediatrics is created, physicians who are not familiar with modern methods will seek postgraduate training to help their patients.

This need for the education of the public is indicated by a recent study of chronically diseased adults who were not receiving medical care;

*Immunization against diphtheria was made compulsory in North Carolina in March, 1939.

80 per cent of them failed to obtain this care through ignorance and the need of education and only 10 per cent because of economic reasons.[7] That public education can be efficacious and that the money for cancer publicity was well spent are demonstrated by the fact that among cancer patients, only 37.4 per cent went without medical care through ignorance and 1.5 per cent for economic reasons.[7] A similar public education campaign for preventive pediatrics should be equally fruitful.

If this program or some modification of it is adopted and is intelligently operated by pediatrically trained physicians, many of the preventive measures recommended[8] will be made effective among the underprivileged one-third of the population for whom the plan was recommended. In addition, the children of the remaining privileged two-thirds of the people also will receive greater preventive care, as a result either of the stimulus or of the extension of the government-aided program.

Although many more children than formerly are getting adequate pediatric care and although there is a much greater number of qualified physicians among whom the patients are divided,[9] this greatly needed increase in preventive pediatrics will necessarily modify the practice of the specialty. The bulk of the care of children and the carrying out of the preventive measures[8] will be and should be in the hands of general practitioners,* now that the teaching of pediatrics has been improved, and the feeding of infants has been simplified. Many of the present pediatrists probably will become salaried members of state and federal health organizations and will be responsible for the supervision and consultation necessary to effectuate the program for the reduction of infant and maternal mortality. This new status of pediatrics will be similar to the changes wrought in private school teaching by the universal public education movement at the turn of the century.

Recent medical graduates who are primarily interested in pediatrics will still have the same four choices of careers, though the proportions will change, i.e., the majority probably now will prepare themselves for general practice instead of going into pediatrics as a specialty, and the minority will become private pediatrists, government consultants, and teachers of pediatrics.

The private practice of pediatrics, though limited by the federal and state child health programs and the better training of general practitioners and medical students, will still remain because children have needs which are different from those of adults. However, the numbers of ill children probably will be reduced through preventive measures.[8] To remain successfully in private practice, the pediatrist must continue to lead in preventive measures and also include mental hygiene and adolescent problems in his field.[10]

The greatest present pediatric need is in rural communities, and it can only be met by encouraging younger well-trained general practi-

*See footnote p. 810, "Abstract From the Recommendations, etc."

tioners to forsake the medically overcrowded cities. Unfortunately, the city youth often is ill-fitted for country life and practice; it is necessary to provide means, probably through loan funds, for the rural student to study medicine.[11] Analyses indicate that the majority of them return to the country.[12] The law of supply and demand is causing a larger percentage of the present graduates to enter general practice, but the number going into rural practice is still falling,[13] except in North and South Carolina. In these two states the establishment of rural hospitals through the aid of the Duke Endowment is improving medical service in the country and attracting young physicians there. In addition, such local hospitals influence older physicians, who have kept abreast of the times, to remain in rural communities.[14] The subsidizing of hospitals and the building of new ones as they are needed, advocated by the Technical Committee on Medical Care,[3] will have a similar result.

REFERENCES

1. Ruhräh, John: Pediatrics of the Past, New York, 1925, Paul B. Hoeber, 592 pp.
2. Davison, W. C.: J. PEDIAT. **9**: 209, 1936; The Mississippi Doctor **13**: 16, 1935; South. M. & Surg. **100**: 457, 1938; J. PEDIAT. **3**: 64, 1933; The Compleat Pediatrician, Duke University Press, Durham, N. C., ed. 2, 1938, 309 pp.
3. National Health Conference, J. A. M. A. **111**: 432, 1938.
4. Eliot, M. M., Bierman, J. M., and Van Horn, A. L.: J. PEDIAT. **13**: 678, 1938.
5. Arena, J. M., and Rasmussen, L. P.: J. PEDIAT. **13**: 352, 1938.
6. Rorem, C. R., and Fischelis, R. P.: The Costs of Medicines, Publications of the Cost of Medical Care, No. 14, Chicago, 1932, University of Chicago Press, p. 18.
7. Lombard, H. L.: J. A. M. A. **111**: 1747, 1938.
8. Davison, W. C.: Preventive Pediatrics (in press).
9. Sweet, C.: J. A. M. A. **111**: 893, 1938.
10. Casparis, H.: Medical Aspects of Child Training (in press).
11. Davison, W. C.: A Survey of Medical Education in the South, Address at the Inauguration of Oliver C. Carmichael as Chancellor of Vanderbilt University and a Symposium on Higher Education in the South, Vanderbilt University, Nashville, Tenn., 1938.
12. Hyman, O. W.: J. A. Am. M. Coll. **12**: 301, 1937; South. M. J. **30**: 85, 1937.
13. Rankin, W. S.: First and Tenth Annual Reports of the Hospital Section of the Duke Endowment. Charlotte, N. C., 1925 and 1934; Mayers, L., and Harrison, L. V.: The Distribution of Physicians in the United States. N. Y., General Education Board, 1925; Rappelye, W. C.: Discussion. Bull. A. Am. M. Coll. **2**: 46, 1937; Weiskotten, H. G.: Present Tendencies in Medical Practice, Bull. A. Am. M. Coll. **2**: 29-47, Jan. 1927, and J. A. Am. M. Coll. **7**: 65, 1932.
14. Rankin, W. S.: Third, Fourth, and Tenth Annual Reports of the Hospital Section of the Duke Endowment, Charlotte, N. C., 1927, 1928, and 1934; also South M. J. **24**: 1113, 1931; J. A. M. A. **92**: 1274, 1929; Duke Endowment Year Book, No. 6, New York, 1937.

Critical Review

TUBERCULOSIS IN CHILDREN

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IS THERE justification for assuming that the problems in tuberculosis have been solved, that the answers to pathogenesis, resistance, immunity, allergy, and many others have been found, and that complete and permanent control of the disease in the human being can be accepted as being definitely assured? How many of the newer ideas and concepts which have been brought forth in recent years are established facts, and how many of them are but ingenious theories to explain unknown processes which will have to be modified as time reveals the true situation? Certainly the literature of the past year leads one to the inescapable conclusion that instead of unanimity of thought, the newer knowledge has only stimulated controversy, created new and unexpected problems, and resulted in expressions of uncertainty and widely divergent opinions. Unquestionably this state of affairs is highly desirable if true progress is to be made, but it is somewhat disconcerting.

For the most part, the conflicting views have to do with various aspects of primary tuberculosis, and particularly with the relation primary infections bear to the development of reinfection tuberculosis. In previous reviews we have attempted to set forth the essentials of the many concepts as they have been published. These need not be repeated here, except for purposes of clarification. Our aim in this review is to continue to present such recent studies and contributions as seem to us to make a point on one side or the other in elucidating some of the more important present-day issues. The first part of the review will deal almost exclusively with primary tuberculosis. We shall also summarize the work which has been done in tuberculin studies.

However, before taking up the review proper, we should like to call attention to two important publications which have been published recently. The first of these is the second edition of *Tuberculosis Among Children and Young Adults*, by J. Arthur Myers.[1] This volume represents a summary of the conclusions which the author and his associates have reached from their many years of longitudinal study for tuberculosis of thousands of children and young adults carried on at Lymanhurst and elsewhere in the University of Minnesota. The contributions which this distinguished group of physicians have made to the better understanding of the evolutionary course of the tubercle have received world-wide recognition, and, while agreement with some of their views has not been universal, nevertheless, the influence of their work in molding thought has been recognized everywhere. Since much of the material in Dr. Myers' book has been previously published in various medical journals concurrently with the progress of his studies and since the essential concepts in these articles have been previously reviewed in these pages, we shall refrain from commenting further upon the subject mat-

ter in this new volume, profitable though that might be. We may add only that the volume affords the practitioner and the student alike a ready source for gaining up-to-date knowledge of the newer concepts in the whole field of tuberculosis, from infancy to old age, and the extensive bibliography appended to each chapter offers a guide to any desired supplemental reading.

The second publication referred to is the eleventh edition of *Diagnostic Standards*[2] published by the National Tuberculosis Association. Instead of being called the eleventh edition, however, this work is designated as the "Tentative Edition—1938." A word of explanation as to the reason for this title is interesting and lends support to the thought expressed in our opening paragraph. The brochure was prepared by a committee of ten expert phthisiologists appointed by the president of the National Tuberculosis Association in 1936. Their original manuscript was submitted to numerous clinicians and further modified according to replies received, but still left certain points in doubt or disagreement. Offered tentatively in its present form, the committee hopes to elicit further comments from specialists, general practitioners, and public health administrators, which "will lead to the formulation of standards and definitions which will be more universally acceptable." Because of the source, the statements made in this booklet are generally accorded an "official" status. Officially then the terms "childhood type" and "adult type" tuberculosis have been dropped, to be replaced by the more satisfactory terms "primary tuberculosis" and "reinfection tuberculosis" respectively. This change is in keeping with clinical experience, in that primary tuberculosis may occur at any age period and reinfection tuberculosis is seen in childhood as well as in adult life. Furthermore, the new terminology coincides with international usage. Physicians should find *Diagnostic Standards* a very useful pamphlet. In condensed form it gives the essential features of both primary and reinfection tuberculosis and the pathogenetic correlations of all forms of tuberculosis. It defines terms, describes technical procedures, and presents a classification and descriptive summary form so framed that it may be adapted readily to any kind or location of tuberculous lesion. These forms may be purchased in quantities from the National Tuberculosis Association or its affiliated associations.

PRIMARY TUBERCULOSIS

Definition.—As has been indicated, much confusion exists in the literature in respect to many phases of the primary infection. In the matter of definition, for instance, there are two rather distinct schools of thought. One group (rather extensive in this country) accepts the viewpoint developed at Lymanhurst by Stewart, Harrington, and Myers.[3] In essence, this concept considers first or primary infections to be those resulting from implantation of virulent tubercle bacilli upon nonallergic soil. When such infections occur in the lungs, the resulting lesions are, first, a primary pulmonary focus (or multiple foci); second, tuberculosis of the associated hilus glands; and third, foci in distant organs as the result of preallergic hematogenous dissemination of bacilli. In a few of the cases, coincidentally with the development of allergy, which takes place in from three to seven weeks after the initial infection, there occurs a collateral inflammatory reaction about the primary pulmonary focus of sufficient size and density to be demonstrable roentgenologically. The invariable course of the lesions of first infection tuberculosis, where

no new postallergic exogenous or endogenous reinfection occurs, is one of slow retrogression, encapsulation, calcification, and in some instances, ossification or complete disappearance of the lesions. First infection tuberculosis is, therefore, considered to be a routine benign disease, regardless of the age at which it occurs. A postallergic extension, or appearance of new tuberculous pathology beyond the limits occupied by the original set of primary lesions, marks the onset of a reinfection type of the disease. Thus, tuberculous meningitis, miliary tuberculosis, and tuberculous bronchopneumonia are regarded as acute manifestations of reinfection tuberculosis, whereas phthisis is a chronic form. Hence, this concept takes into account the part played by allergy in the production of all the serious and fatal forms of tuberculosis.

The opposing group draws no such line between the primary infection and the acute reinfection forms. *Diagnostic Standards* states, "By 'primary tuberculosis' is meant the totality of the morbid processes following directly and uninterruptedly the first implantation of tubercle bacilli. It is obvious that in many instances no sharp line of demarcation can be drawn between primary and reinfection tuberculosis. To say that the appearance of allergy marks the end of primary tuberculosis (as is frequently suggested) would mean that no clinically recognizable and diagnosable phase of tuberculosis could be so designated." While the most frequent development of the primary complex is one of slow retrogression, in a minority of cases, the percentage of which is hard to estimate, and particularly in infants and in children exposed to prolonged infection, and more frequently in colored than in white children, the primary complex does not heal promptly but becomes progressive. Progress may occur at the site of the primary pulmonary focus leading sometimes to a large excavating pneumonia, or the progressive primary focus may rupture into a bronchus with resulting bronchogenic spread. Similarly primary lymph node lesions may progress to rupture into a bronchus, or bacilli may finally reach the circulation through efferent lymph channels to proximal lymph nodes. Transported by the blood, the bacilli may cause single or multiple lesions in the lungs, meninges, bones, kidneys, and other organs. Thus miliary tuberculosis, tuberculous meningitis, and tuberculous brochopneumonia in this concept are considered as being part of the primary infection. Viewed in this light, first infection tuberculosis is by no means a benign disease. In a further analysis of the differences in opinion, two significant points need to be stressed. In the Lymanhurst concept the fundamental difference between primary and reinfection tuberculosis is allergy. In the viewpoint as defined in *Diagnostic Standards,* the difference between the two is in the manner of progression of the lesions. The differences are clearly brought out by quoting a statement from Pinner,[4] who says: "In the progression of tuberculous lesions is found, probably, the clearest expression of the differences between primary and secondary infections. The functional difference between the two is allergy. Pathogenically the differences are that in the progression of a primary lesion all available routes of propagation of bacilli come into play: lymphatics, blood stream, preformed channels. In secondary infection, dissemination through the lymph and blood stream is quite infrequent, increasingly so with the increase of time elapsed between primary and secondary infection. Progression by continuity and through preformed channels is common in secondary infection. Thus as a characteristic example of progressive disease following more or less closely upon primary infection

is seen generalized miliary tuberculosis, frequent in childhood, rare in later life. The characteristic progressive disease of adult life is tuberculosis limited to one organ system, such as pulmonary phthisis, rare in childhood, frequent afterward."

The definition of primary tuberculosis, as contained in *Diagnostic Standards*, to the effect that the appearance of allergy marks the end of the primary infection, seems susceptible to challenge. We are aware of no such viewpoint. If, as we suspect, the reference is to the Lymanhurst view, it is a misconception of this idea. The appearance of allergy marks the end of the period when new exogenous or endogenous infections react as do primary infections, but the original first infection which produced the allergy, unless interrupted by death, will retain the characteristic features of the primary complex through all the stages of resolution and calcification, regardless of superimposed secondary infections. In other words, primary complex and primary infection are essentially synonymous terms in this concept.

Carroll[5] from the Undercliff Sanatorium for Children in Connecticut, after observing some 3,300 children over a period of seventeen years, states that he has reached much the same conclusions regarding tuberculogenesis as have Myers, Stewart, and their associates at Lymanhurst. He believes it to be "a fundamental principle that tuberculous lesions arising in allergic and in nonallergic tissues have vastly different clinical expressions." Pathologists, on the other hand, seem more inclined to the view that, while it is usual, it is not an invariable rule, for the lesions of the primary complex to progress to anatomic healing. Auerbach,[6] pathologist at the Sea View Hospital in New York, reports seventeen cases autopsied in a period of four years, in which progression occurred in the primary complex. With one exception the children were negroes; fifteen of them were between the ages of 1 and 3 years. The author describes the various degrees of caseation, liquefaction, and cavitation encountered, and explains the pathologic features which serve to differentiate primary from tertiary excavations. Macgregor and Alexander[7] of Edinburgh, on the basis of some two hundred pathologic examinations of cases of primary thoracic tuberculosis, describe the various modes of origin of localized extension and widespread dissemination from the primary lung complex. That the point of view is not one to be easily settled, even by workers of such extensive experience, is shown by the following quotation from this article, "When there is severe and widespread pulmonary tuberculosis, the question arises of what part, if any, is played by repeated exogenous reinfection in the pathogenesis of the disease. Does the whole trouble arise from the progressive spread of infection from a single primary focus, or are new infections from without responsible for at least a part of the widespread dissemination? The question is difficult to answer with any certainty. On the one hand, it is often possible to trace, with at least a fair degree of plausibility, the progressive evolution of the pulmonary lesions from their origin in the primary focus. On the other hand, many children who develop this grave type of pulmonary tuberculosis have been exposed to the risk, or indeed the certainty, of repeated heavy infections, perhaps from a tuberculous mother or other member of the household."

Perhaps sufficient has been said to establish the point that confusion exists regarding the delimitations of primary infections. The problem would seem to be of some importance, for to one group the primary infection is a benign form of tuberculosis seldom resulting in disease

or death, while to another group it is a serious disease accounting for practically all the deaths from tuberculosis in early childhood. Perhaps it is more a matter of definition than anything else, but even so it would be advantageous if everyone "talked the same language."

Endogenous Reinfectivity.—Another controversial subject has received renewed impetus as the result of the report by Feldman and Baggenstoss[8] upon the residual infectivity of the primary complex. Heretofore, wide acceptance has been given the opinion that tubercle bacilli may remain viable in the centers of the calcified pulmonary and lymph node foci of first infection tuberculosis for many years, and possibly throughout the lifetime of the individual. The persistence of a positive reaction to the tuberculin test in otherwise healthy persons is most frequently explained on the basis of continual production of tuberculoprotein from bacillary activity within the lesions of the primary complex. Those who contend that the pathogenesis of reinfection tuberculosis may have an endogenous source assume the latency of the lesions of the primary complex or of the secondary hematogenous foci established in the preallergic postinfectious period. Thus Myers[1] from his long experience at Lymanhurst has frequently referred to the primary complex as being a double liability, in that it first creates tuberculo-allergy, and then for years after harbors a potential source of living organisms which may at any time become liberated to set up a focus or foci of reinfection tuberculosis. In support of this view he has pointed to the work of Robertson,[9] of the Mayo Clinic, who concluded after an extensive study of autopsy material that apparently healed tuberculous lesions may become clinically active after varying intervals. Wallgren,[10] whose opinion is probably representative of continental Europe, even goes so far as to maintain that pulmonary tuberculosis is always of endogenous origin, although not necessarily from the primary complex. He believes that in tuberculosis, as in syphilis, a primary infection establishes an immunity which is effective against all ordinary exogenous reinfections, but not against extensions of the disease already present within the body. In his judgment, most often pulmonary tuberculosis arises from secondary hematogenous foci in the lung (escapes from the primary complex) in those individuals who possess a special disposition to tuberculosis, and who have reached the age of puberty. Thus many competent observers are convinced of the truth of the statement, "once tuberculous, always tuberculous."

Now, however, Feldman and Baggenstoss, also of the Mayo Clinic, have most carefully examined a total of 103 specimens obtained from 68 unembalmed bodies of human beings who died from causes other than tuberculosis and have found viable tubercle bacilli in only one instance! Forty-one of the specimens were from Ghon tubercles, fifty-five from hilar lymph nodes, five from apical scars, one from a mesenteric lymph node, and one from a tuberculous thymus gland. The ages of the individuals varied from 7 to 90 years, the greatest number being in the fourth, fifth, and sixth decades. Eight tubes of culture material and two guinea pigs were inoculated with emulsified material obtained from each lesion. The authors believe the methods employed in the study were such that if live organisms had been present they would have been found. The one positive result was obtained from an encapsulated caseocalcareous Ghon tubercle in the right lung of a man 54 years of age. A Ghon tubercle in the left lung gave negative results. Feldman and Baggenstoss conclude that "in adults, endogenous rein-

fection is unlikely to occur from lesions of the primary complex." It is doubtful if this important and excellent study will be generally accepted as having offered convincing proof of the conclusions reached. As stated in a recent editorial,[11] it does prove beyond question that the lesions of the primary complex may and do heal completely, and to this extent refutes the assertion "once tuberculous, always tuberculous." However, on the basis of the limited scope of the authors' investigation, further conclusions are probably not justified. All the individuals studied were admittedly free from gross tuberculous disease. Would an equally careful search for organisms in a group of individuals with active pulmonary disease give the same negative results? May it not be that the reason for the absence of active tuberculous disease in the bodies examined was that the lesions of the primary complex had become sterile? Furthermore, the report does not consider the possibility of endogenous reinfection as maintained by Wallgren. Without question this work by Feldman and Baggenstoss will stimulate many other investigators to study the problem from all angles, with the desirable prospect that the near future will bring clarification to the present muddled situation of exogenous versus endogenous reinfection.

Healed Primary Complex.—Before leaving the subject of healing in the lesions of the primary complex, there is another closely related phase of the problem which merits attention. This has to do with loss of hypersensitivity in individuals previously known to have reacted positively to the tuberculin test, and with unmistakable x-ray evidence of tuberculous lesions in individuals who react negatively to maximum doses of tuberculin. It is usually stated that healthy individuals previously infected with tuberculosis will react positively to the tuberculin test if 1 mg. of old tuberculin or the second dose of purified protein derivative is used. A negative test with these doses is generally accepted as excluding tuberculosis. From recent data obtained in retesting surveys, evidence is accumulating that this may not be entirely true. For instance, Tortone, Chattas, Myers, Stewart, and Streukens,[12] in a study of tuberculosis in Lymanhurst children under six years of age, report that during the course of a follow-up study twenty-two children who previously were sensitive to tuberculin later lost their sensitivity and gave negative reactions to repeated intracutaneous injections of 1 mg. doses of old tuberculin.

Rich[13] cites the reports of Lloyd and MacPherson from England, who found that of 303 healthy London children who reacted to 1 mg. of old tuberculin in 1930, 2 per cent were negative to that dose two years later; of Aronson who followed 87 tuberculin-positive urban children for a period of five years, during which time 9 per cent became negative to 1 mg. of old tuberculin; of Horan who tested 197 adolescent boys yearly for three successive years and found that 14 per cent of those positive on the first test lost their sensitivity; and of Paretzky who reported that of a group of tuberculin positive children followed up to five years, 80 became negative to 1 mg. of old tuberculin, and 64 per cent of these failed to react to 10 mg. of old tuberculin. Rich also cites the following reports of tuberculous lesions demonstrable by x-ray in persons who reacted negatively to tuberculin. Barnard, Amberson, and Loew found that of 184 school children between 12 and 15 years of age who had tuberculous lesions demonstrable by x-ray, 6 per cent failed to react to 1 mg. of old tuberculin. Wells and Smith found

demonstrable x-ray lesions in 5.5 per cent of 128 individuals who presented negative reactions to 1 mg. of old tuberculin. Opie and his associates showed that 15 per cent of 186 children between the ages of 5 and 19 years who were negative to 1 mg. of old tuberculin had definite x-ray evidence of tuberculosis. Crabtree, Hickerson, and Hickerson found 17 per cent of a group of persons over four years of age who were negative to 1 mg. of old tuberculin to have calcified lesions on x-ray examination.

The implications of these findings raise many interesting speculations. If one believes the persistence of tuberculin sensitivity to be due to viable tubercle bacilli in the primary complex, then these clinical observations lend direct support to the results obtained by Feldman and Baggenstoss at autopsy: that a certain number of primary complexes will undergo complete healing. However, if one believes that persisting sensitivity results from repeated small exogenous reinfections, one must consider whether the marked decline in morbidity and mortality rates from tuberculosis may not be playing an important part in its loss by greatly reducing the opportunities for chance contact with tubercle bacilli. At any rate, it appears certain that a proportion of the population who have experienced primary tuberculous infections, but who are no longer allergic as measured by the tuberculin test, will reach adult life. What form will subsequent tuberculous infections take in these individuals? Will they follow the characteristics usually associated with primary infections; namely, a pulmonary focus located anywhere in the lung, marked involvement of associated lymph nodes, and a strong tendency to retrogression by encapsulation, calcification, and ossification; or will they follow the reinfection type of disease characterized by apical or subapical parenchymal lesion, little or no involvement of associated lymph nodes, prominent fibrosis, and a tendency to caseation, liquefaction, excavation, and bronchogenic spread? The longitudinal observation of the fate relative to tuberculosis of such persons offers an opportunity to shed light upon the obscure relation now existing between allergy and immunity or resistance. If allergy and immunity are identical, it would seem logical to suppose that they would again undergo a primary infection if sufficiently exposed to produce disease. On the other hand, if the disease process followed the pattern of reinfection tuberculosis, it would be strong evidence of resistance remaining even though allergy had been lost. To the best of our knowledge, no reports have appeared in the literature of observations made under these exact conditions.

Primary Infections in Adults.—Reports are appearing concerning the clinical and pathologic aspects of the type of tuberculosis developing in young adults who have not previously experienced known primary infections. Here again we run into decidedly conflicting viewpoints. It is interesting to compare what such unquestioned authorities as Rich,[13] Myers and co-workers,[14] and Sweany[15] have to say on the subject. All agree that a changed situation in the civilized world has taken place in recent years. Formerly it was probably true that the majority of persons had received primary infections by the time they reached young adult life; today, tuberculin surveys indicate that the rate of infection has fallen to such a degree that from one-half to three-fourths or more of young people are reaching high school and college age without having been infected. Rich maintains that if more than half of the present crop of young adults have grown up uninfected, we should be encoun-

tering on all sides many instances of primary tuberculosis demonstrable both clinically and pathologically, but that such is not the case. "Young adult tuberculosis, both at the bedside and at the autopsy table, has today precisely the same characteristics as that during the period when primary infection in urban adults was almost universal." He points out that in other countries (Sweden and Germany), apparently true cases of primary tuberculosis in adults have been observed. He concludes "that either our long held concept of the pathogenesis of adult type tuberculosis requires a drastic revision, or else that many individuals who today are tuberculin negative have really been infected, and have retained their acquired resistance to the degree that determines the peculiarities of adult type tuberculosis, but have lost their hypersensitivity and under present conditions of diminished opportunity for reinfection they remain tuberculin negative for longer periods than would have been the case formerly."

Myers and his co-workers,[14] on the contrary, are convinced from their observations on students of medicine and nursing that primary tuberculosis does occur in young adults and that it runs the same course and has the same characteristics as the disease in infants and children. They cite one school of nursing with a tuberculosis service in which approximately 22 per cent of the students entering as probationers reacted positively to the tuberculin test, but on graduation 94 per cent gave positive reactions. Under such conditions they have had an opportunity to observe shifts from negative to positive reactions within relatively short periods of time. Furthermore, x-ray studies made on such positive reactors have usually been negative. In the occasional instances in which the x-ray film has revealed the site of the primary focus in the lung, the lesions have been observed to persist for many months, with no signs of illness, and eventually to resolve or disappear altogether. Commenting further, the authors say, "Some have suspected these shadows to be caused by reinfection type of lesions because some of them are located in the subelavicular region. Such interpretations are based on the assumption that all young adults have been previously infected and later lost their allergy. We have not been able to obtain any evidence to substantiate such an assumption. Since only approximately 1 per cent of the population becomes infected each year in the community investigated, this fact does not permit us to assume that 100 per cent of the young adults we have observed have been previously infected. To us, the location of the lesion is no criterion as to its type, since we have repeatedly seen the first infection type of tuberculosis in children appear in the apex or subelavicular region, as well as the basal parts of the lungs." In addition, the authors state they have seen reinfection tuberculosis appear in a number of the young adults who developed primary complexes while under observation, months or years after the first infection type of disease was discovered.

Sweany,[15] pathologist at the Chicago Municipal Tuberculosis Sanitarium, presents a view midway between that of Rich and the Lymanhurst group. He finds that because of the reduced infection rate many more people are receiving their primary infection in adult life but that these primary infections are not recognized as such because they are frequently atypical. One of these atypical features is that the primary lesion tends to become more localized in the parenchyma of the lung, but overflows into the surrounding tissues by a direct chain of colonies to set up an area of reinfection tuberculosis, and this within a

much shorter space of time than usual. Only by careful study can the primary infection be distinguished from the reinfection type. A second atypical feature is the lymph node involvement, the extent of which is not nearly so great in cases of adult primary tuberculosis as in childhood tuberculosis. Sometimes the nodes of the hilum are not even reached. Herein, perhaps, lies the explanation for the infrequency of hematogenous spread (meningitis) of the tubercle bacilli in adults as compared with infants and children. Sweany conjectures that the lessened involvement of lymph nodes may be due to changes in the lymphatic anatomy as the individual advances in age or that some nonspecific factor acquired from other infections may localize the germs and prevent their free spread by the lymphatic system. His conception is then that the pattern of primary tuberculosis follows the typical course in infants, children and primitive adults, but that in civilized adults, it tends to take on many of the features of reinfection tuberculosis, but is distinguishable from the latter.

Mortality.—There is yet another phase of primary tuberculous infection about which agreement is conspicuously lacking. This has to do with the mortality rate suffered by infants and children who become infected with the tubercle bacillus for the first time. However, this applies only to the age period under 5 years, and more particularly to the period of infancy, from birth to 2 years of age. There is no disagreement that the "safest" period in the entire life cycle as far as risk to life from tuberculosis is concerned, is from 5 years to puberty. Rich[13] states that "by far the most dangerous age period in which to be infected, from the standpoint of the chance of succumbing during that age period, is that of the first five years of life, and most particularly during the first year." Myers,[1] on the other hand, declares that after fifteen years of observation he finds "a very small percentage of the infants who had first infection type of tuberculosis died of that disease in infancy or early childhood." Several studies bearing on the topic are available for reference.

Dorothy Price,[16] of Dublin, reports on the outcome in 78 cases of infants suffering from tuberculosis. Of these patients, 60 or 77 per cent have died, and 18 or 23 per cent recovered. Twenty-two of the deaths resulted from caseous pneumonia spreading from broken down primary foci; 18 from miliary tuberculosis; and 17 from tuberculous meningitis. In addition, there were two deaths from abdominal tuberculosis and one from congenital tuberculosis. Of the 18 patients who recovered, all had a history of family contact, all had positive tuberculin tests, and all had positive pulmonary x-ray findings. Eight of the infants were under 6 months of age when first observed. This study contributes little in supplying an answer to the question of how infants tolerate tuberculous infections, for it merely represents a collection of the majority of the infants in Dublin who developed manifest signs of illness. One would like to know how many other infants in Dublin in the same age period were infected, but did not come under observation, presumably because no signs of illness developed. The report of the 18 children who recovered, although parenchymal disease was demonstrable, furnishes indisputable proof that tuberculous disease in infancy is not necessarily fatal, as was at one time held to be the almost universal rule.

Braily's observations[17] on the course of tuberculous infections in infants and children carried on for a period of eight years at the Harriet

Lane Tuberculous Clinic in the out-patient department of Johns Hopkins Hospital, supply a most reliable and significant source of information regarding the problem under discussion. A total of 223 children, of whom 91 were white and 132 colored, are included in the study. All of them were found to be tuberculin positive before 2 years of age. Only 9, or 10 per cent, of the 91 white children have died in the eight years of observation. Eight of the deaths occurred within the first year from discovery of the infection, and one additional death occurred in the first five-year period. Thirty-two of the white children showed a parenchymal lesion on the first x-ray examination, and eight of the deaths occurred in this group. Only one death from tuberculosis occurred among the 59 white children whose first x-ray examination showed no parenchymal lesion. One additional fact of importance is that infants known to be infected before 6 months of age had a mortality rate nearly twice as great as children found to be infected between 6 months and 2 years of age. The colored children in Braily's series did not fare as well as the white children. Not only was the mortality rate among them more than three times as high, but they also showed a greater tendency to develop parenchymal lesions, a fact which undoubtedly explains the increased risk to life.

A study equal in value and merit with that of Braily's is one by Tortone, Chattas, Myers, Stewart, and Streukens[12] on the fate of 629 Lymanhurst children under six years of age, known to be infected with tuberculosis and followed over an average period of five years. Ten, or 1.6 per cent, died from tuberculosis. Pneumonic infiltrations characteristic of the acute stage of primary pulmonary tuberculosis were demonstrable roentgenologically in 155 of the children; 268 had normal chest films; and the remainder showed calcification, either as Ghon tubercles or in the hilus lymph nodes, or both. Nine of the ten deaths occurred among the group with pneumonic infiltrations which did not form Ghon tubercles. One child in the age period from 1 to 2 years with calcified hilus glands died, presumably of tuberculosis. Five or 9.6 per cent of the 52 children in the group under 1 year of age died, and five or 3.8 per cent of the 132 children in the age group from 1 to 2 years of age died. No deaths occurred in later age periods.

If only the white children are considered, the experiences at the Harriet Lane Clinic and at Lymanhurst have been strikingly similar. The studies justify the drawing of fairly definite conclusions relative to infants and young children infected with tuberculosis.

1. At least 90 per cent of white children infected with tuberculosis within the first five years of life may be expected to survive their tuberculous infection.

2. Such mortality as there is will be almost entirely confined to the first two years of life.

3. The risk to life is over twice as great in infants who become infected in the first year of life as in infants who do not become infected until the second year.

4. The great majority of all tuberculous deaths will occur among the group of infected infants whose chest roentgenograms reveal a parenchymal lesion.

If further proof is desired of the ability of infants to resist severe tuberculous infection, one needs only to recall the unfortunate occurrence at Lubeck in 1930, when by error 251 newborn infants were given

virulent tubercle bacilli, instead of the supposedly avirulent Bacillus Calmette Guérin culture. Seventy-two of the infants died of extensive tuberculosis in the first year, but the remainder, or 71 per cent, resisted the infection.

Immunity.—A final point of particular interest is the question of the immunizing effect (or lack of it) of primary infections. Here again diametrically opposed opinions are freely expressed. One school holds that primary infections, successfully withstood, impart an immunity which is effective in preventing all subsequent ordinary reinfections. As proof of their contention, they point out that while 50 to 60 per cent of the adult population are infected, only about 1 per cent ever develop clinical disease. The opposing group believes that primary infections not only fail to immunize but that on the contrary they furnish the essential prerequisites which lead to the development of reinfection tuberculosis, namely, allergy and a potential source of tubercle bacilli. Ch'iu, Myers, and Stewart[18] submit a study in support of the latter viewpoint. During the eight-year period from 1921 to 1928, 446 positive and 772 negative tuberculin-reacting children came under observation at the Lymanhurst Health Center. The positively reacting children were followed for an average of 11.3 years, and the negative reactors for an average of 10.95 years. The average age of the former when first seen was 7, and of the latter 6.6 years. At the end of the observation period it was found that 67, or 15.02 per cent, of the 446 positive tuberculin reactors had become ill with reinfection type of disease, while only 13 or 1.68 per cent of the 772 negative reactors had developed clinical disease. There were 22 deaths among the former group and only 1 in the latter, giving a mortality ratio of positive and negative reactors of 38 to 1. Thus the study shows that tuberculous disease developed nine times more frequently among the positive reactors than among the negative ones. Commenting on their findings, the authors state, "With 15 per cent of the children who reacted positively to the tuberculin test, with no other findings of clinical disease, falling ill within approximately the next ten years, it is obvious that a tuberculin reaction in a child is of far more significance than we formerly believed. If the morbidity and mortality continue among the individuals throughout the span of life as they have begun, clinical tuberculosis will be as frequent among them as is tertiary syphilis among previously positive Wassermann reactors. This would seem to be sufficient evidence to dispel any great enthusiasm for immunity produced by the primary tuberculous complex. Indeed, by our old criterion this is the group that should have been immunized by reason of infections in childhood. One might maintain that the remaining 85 per cent have been immunized, but any argument in this direction at present would be nothing more than speculation; only time will tell, and, since no observations have previously been made, it would be futile to venture an opinion. Suffice it to say that 15 per cent is a large toll to be exacted in so short a time."

TUBERCULIN STUDIES

The importance which tuberculin testing has come to assume in the campaign for the control of tuberculosis has led to the undertaking of many valuable studies, both laboratory and clinical, concerning tuberculin and its use. Some of the more significant of these studies are summarized in the following paragraphs.

One of the most startling contributions is that of Gruskin, Louria, Bennett, and Schwartz[19] of Temple University, who introduced an intradermal test for the determination of activity of tuberculosis. The test is based on the reaction to homologous proteins comparable to the intradermal tests for malignancy and pregnancy. The mechanism of the reaction consists in the intradermal injection of antibody (homologous protein), and depends upon the antigen formed within the organism during the active phase of the disease responding by the formation of pseudopodia. An extract of fibrin, obtained from guinea pigs which have been previously injected with a suspension of tubercle bacilli, is the material employed in performing the test. The test is read within three to five minutes after the injection and is considered positive if pseudopodia appear. The authors report from 92 to 96 per cent positive skin tests in some five hundred cases of active pulmonary tuberculosis proved by x-ray, sputum examination, or guinea pig inoculation. Positive tests were also found in a small series of cases of extrapulmonary tuberculosis. Negative tests were recorded in a few pathologic states which were not tuberculous. Obviously, a test which would differentiate between active and inactive tuberculosis would be a most valuable addition to our diagnostic armamentarium. However, the value of the test advocated by Gruskin and his co-workers must be subjected to a much more severe application before any appraisal of its value can be made. Certainly future experiences with the test will be watched with a great deal of interest.

The possibility that tuberculin used in making tests may in itself induce hypersensitivity so that subsequent tests give rise to false positive reactions has received considerable attention in the past. Seibert[20] has shown that the sensitizing potentialities of the various tuberculoproteins are related to their molecular weights. Thus MA-100 with a molecular weight of 26,000 sensitized nontuberculous animals, whereas purified protein derivative with a molecular weight of 2,000 to 3,000 did not do so. In a very careful and exhaustive study, Nelson, Mitchell and Brown[21] sought an answer to the question, "Is tuberculin, in amounts ordinarily used for skin testing, capable of producing sensitization to itself in man, and if so, do different tuberculins vary in this respect?" Some 800 children were employed in the study varying in age from young infants to children ten years of age and over. Selection was made on the basis of negative reactions to two preliminary screening tests. The material used was MA-100, old tuberculin, and purified protein derivative. In order to cover as many possibilities as desired and to facilitate comparison, the children were divided into four groups. Roentgenograms of the chest were made on approximately one-half of the children. As many as fourteen tests, made with each of the three materials and at varying intervals, were given in some of the groups. A reacting area of 5 mm. or more in diameter was considered positive. A considerable number of the children reacted to the third test which was performed four days after the first test. However, the authors conclude it does not appear probable that sensitization to tuberculin was induced because "first, of the fact that the third injection was performed 96 hours after test one, an interval presumably too short to permit induction of sensitization; second, of the marked individual inconsistencies in the various series of tests; third, of the failure to develop increasing rates of response or to secure increasingly larger reactions in the individual child; fourth, of the roentgenologic evidence of previous tuberculous

infection in children who, although they did not react to the first two tests, did have reactions larger than 5 mm. of edema in one or more of the subsequent tests; and fifth, of the similarity of 24 and 48 hour responses to 0.005 mg. of purified protein derivative of children who had had repeated injections over a period of two years with that of a group in the same institution who had no reactions to a test 48 hours previously with 0.00002 mg. of purified protein derivative, but who had not had repeated injections."

Another practical study regarding the use of tuberculin is contributed by Lincoln, Raia, and Gilbert,[22] of Bellevue Hospital. In the first place the authors agree with the conclusion reached by Nelson, Mitchell, and Brown, that sensitization to tuberculin from repeated injections is not likely to occur. They gave from four to seven injections of old tuberculin in the same site at two- to five-day intervals to children negative to tuberculin, and failed to get any false positive reactions. Next they attempted to correlate the size and intensity of the tuberculin reaction with the localization of the lesion, the activity of the lesion, and the prognosis of the case, but concluded that no proof of any correlation could be advanced. The stability of dilutions of old tuberculin was investigated. Eight out of eleven children reacted positively to a two-year-old dilution of 1:10,000, although all of the children reacted positively to a fresh dilution. A six-month-old dilution kept outside of the refrigerator resulted in the same number of positive reactors in forty children as a freshly prepared dilution. They conclude that dilutions of old tuberculin up to 1:10,000 need not be prepared oftener than once a month and need not be kept constantly in a refrigerator.

The necessity for the use of separate syringes for tuberculin testing is indicated by an experiment which demonstrates that tuberculin is thermostable. Syringes were filled with a fresh solution of 1:10,000 of old tuberculin and the contents expelled. The syringes were boiled for five minutes, and then filled with a salt solution. Intradermal injections of 0.1 c.c. of the salt solution in twenty children resulted in positive reactions in 40 per cent of the cases. Comparable results were found when the syringes were rinsed ten times in 95 per cent alcohol and three times with normal saline solution. Contrary to the findings of certain other investigators,[13] Lincoln and co-workers are of the opinion that a positive tuberculin test, especially when a diagnosis of primary tuberculosis has been established, rarely tends to become negative during childhood. They retested 113 positively reacting children after intervals of five to twelve years and found that 111 of them remained positive, and furthermore that 99 reacted to the initial dose of 0.01 mg. Since a child with a positive tuberculin test is likely to remain positive during childhood, they see no advantage in repeating the test; in fact, they feel repetition may be definitely harmful. Again differing from some other reports,[13] the authors found only two negative reactions among 352 children with definite roentgenologic or clinical evidence of active or healed tuberculosis. They conclude that a negative tuberculin test is of great significance in excluding tuberculosis in children and that the association of a negative tuberculin test with a healed lesion is uncommon before 12 years of age. They compared the incidence of positive reactions at Bellevue Hospital for the period from 1921 to 1928 and for the period from 1930 to 1936, and report a marked decrease in the first year of life, as well as an appreciable decrease be-

tween the ages of 1 and 2 years, but found the percentage of reactions for all ages had decreased only from 17.0 to 16.4 per cent.

A qualitative and quantitative comparison of old tuberculin and purified protein derivative with roentgenologic correlation on 1,003 children by Crimm, Short, and Wood[23] presents many interesting findings. Each patient was first tested simultaneously with 0.1 mg. of old tuberculin, and 0.00002 mg. of purified protein derivative, and five days later with 1.0 mg. of old tuberculin and 0.005 mg. of purified protein derivative. The result of tests with the first dilutions was the finding of 215 reactors. Of this number, 93 per cent reacted to purified protein derivative, and 76 per cent to old tuberculin, indicating that the former is 17 per cent more effective. With the second dosage there were 325 positive reactions, indicating a superiority over the first dose of about 33 per cent. Of the 325 reactors, 84 per cent reacted to purified protein derivative, and 73 per cent to old tuberculin. From their study the authors conclude that purified protein derivative is 14 per cent more effective in finding tuberculosis than is old tuberculin. Furthermore, the intensity of the reaction to purified protein derivative is usually one to two degrees greater than with old tuberculin. In their opinion the strength of the second dose of purified protein derivative should be diminished. One surprising result recorded in this study, and one quite at variance with most other studies of a similar nature, was that more cases of primary tuberculosis were found in the group of 1,003 children by the x-ray film than by the tuberculin test; 345 of the children had positive x-ray findings, but 153 of them reacted negatively. The majority of the anergic cases occurred in the group from 8 to 14 years of age.

Opinion is nearly universal that the intradermal method of tuberculin testing possesses advantages which make it superior to other methods. However, circumstances may arise in which it is desirable to avoid the use of a syringe and needle. In 1937 Vollmer and Goldberger[24] introduced a patch test for tuberculosis which conformed with the Pirquet test in 85.5 per cent of 209 tuberculous children. Recently these authors[25] have increased the sensitivity of the patch test by the use of tuberculin produced from a synthetic medium which is about four times stronger than the tuberculin formerly used. In a rather small series of cases they demonstrate that the improved patch test conforms to the Mantoux test using the second strength of purified protein derivative. Steele and Willis[26] also found that purified protein derivative and TPT used in a strength of 10 mg. per cubic centimeter gave reactions by the Pirquet method in approximately the same incidence as does old tuberculin used intradermally. One of the surprising recommendations in the use of diagnostic tuberculin is that of Paretzky,[27] who advises the use of 10 mg. of old tuberculin in selected cases. In patients with a suggestive history and suspicious physical findings who fail to react to 0.1 mg. and 1.0 mg. of old tuberculin, the use of 10 mg. not infrequently aids in establishing a correct diagnosis. The author does not recommend this dosage as a routine procedure, only for certain diagnostic problems in which repeated tests with smaller doses are negative.

Of interest in the evaluation of the tuberculin reaction is the work of Howe,[28] who demonstrated a marked daily variation in the reactions of four patients with pulmonary tuberculosis, and of two controls with positive reactions but no roentgenologic or clinical evidence of tuberculosis. Daily fluctuations varying from 100 to 50 per cent of the maximal reaction to the doses employed were recorded graphically. The author

points out that there is a definite correlation between the quantitative variations in the tuberculin reaction and the state of the peripheral vessels as measured by daily diastolic blood pressure levels. Periods of peripheral vasoconstriction are accompanied by decreased reaction to tuberculin. Periods of peripheral vasodilatation, with a falling diastolic pressure, are accompanied by an increased reaction to tuberculin. In the six patients studied, the trend of the tuberculin reaction was roughly parallel; this was attributed to changes in the meteorologic environment.

This year's review may be brought to a conclusion by a brief reference to another interesting study in which the use of tuberculin played a major role. Stewart,[29] looking toward the eventual eradication of human sources of tuberculosis contamination, as has been accomplished by the veterinarians in the bovine family, undertook a study in which the objective was to determine an economical method for detecting households which harbored patients with cases of open tuberculosis. He points out that the ideal and complete method for controlling tuberculosis in man should include, "first, the routine application of the Mantoux test to the present and future members of the entire population; second, periodic retesting of all persons found uninfected on previous surveys; third, frequent roentgenologic, clinical and laboratory examinations of each infected patient discovered during repeated epidemiologic surveys; and fourth, prompt segregation of all patients with tuberculosis until their condition is no longer infectious." While such a program is ideal and not altogether impossible of attainment, it is obvious that for many reasons, the most important of which is economic, little prospect exists of even partial realization of this ideal approach to the control of tuberculosis.

A substitute method is suggested, therefore, which is both economical and practicable; one which, if generally participated in by the practicing physicians of the country, would constitute an epidemiologic control program for tuberculosis among human beings comparable to that which has been established by veterinarians for animals. The economic expedient proposed hinges upon the assumption that any adult members of a household who are sources of contagion will infect the children of that household. Hence, when the Mantoux tests of the children of a family are negative, it can be assumed, even if one or more adults have positive reactions, that the adult positive reactors are not spreaders of tubercle bacilli at that time, and, therefore, relatively expensive roentgenologic, clinical, and laboratory examinations for this group may safely be deferred. All such households can be safely accredited as contagion-free units solely upon the results of the Mantoux tests. Only in those households where one or more of the children react positively to the tuberculin test is it imperative that the infected adults (as shown by positive Mantoux tests) receive these additional examinations.

In a practical demonstration of his plan, Stewart investigated, wholly or in part, the personnel of 642 homes. Approximately 57 per cent of the parents and 84 per cent of the children were given the Mantoux test. Positive tests were found among 57.3 per cent of the parents, and 5.2 per cent of the children. From this and other data obtained in the study, the author concludes that "primary tuberculosis, the type or stage of the disease that is present in each tuberculin-sensitive patient, is a relatively unimportant source from which infection in man is acquired by contact. Apparently efforts to control the human source

of the disease can be concentrated almost exclusively on the identification and segregation of patients with the ulcerative or reinfection type of pulmonary tuberculosis.'' The entire personnel of 213 of the 642 homes was given the tuberculin test. Forty-two of these households did not contain an infected member, and, in 149 more, tuberculin sensitivity was limited to the adult members of the family. Thus 191, or 89.7 per cent, of the completely tested units were tentatively rated as safe for children to live in, this rating being made solely on the basis of the reaction to tuberculin. In the remaining 22 households, the infected members received roentgenologic, clinical and laboratory examinations. The source of the child's infection in only 2 instances was found to be among the 22 homes.

In the present confused state regarding the relative merits of various types of case-finding surveys, Stewart's proposal deserves careful consideration. Sooner or later the futility of haphazard tuberculin surveys, particularly those limited to grade school children, as a means of detecting unknown cases of open tuberculosis, must be recognized. Ultimate success in the epidemiologic control of tuberculosis would seem to depend upon the general adoption of some systematic method of investigation which would eventually include the majority of the people in a given community. It is conceivable that a program aimed at the accrediting of homes, then of counties, and finally of states, might be found as feasible for man as the similar approach has been for animals.

REFERENCES

1. Myers, J. A.: Tuberculosis Among Children and Young Adults, Springfield, Ill., 1938, Charles C. Thomas.
2. Diagnostic Standards (Tentative Edition—1938). Published by the National Tuberculosis Association.
3. Stewart, C. A., Harrington, F. E., and Myers, J. A.: The Lymanhurst Classification of Tuberculosis, Am. Rev. Tuberc. **30**: 588, 1934.
4. Pinner, M.: Pathogenesis of Tuberculosis, J. A. M. A. **107**: 475, 1936.
5. Carroll, W. E.: Early Primary Pulmonary Tuberculosis, Am. Rev. Tuberc. **38**: 190, 1938.
6. Auerbach, O.: The Progressive Primary Complex, Am. Rev. Tuberc. **37**: 346, 1938.
7. Macgregor, A. R., and Alexander, W. A.: Pulmonary Tuberculosis in Children, Edinburgh M. J. **44**: 561, 1937.
8. Feldman, W. H., and Baggenstoss, A. H.: The Residual Infectivity of the Primary Complex of Tuberculosis, Am. J. Pathol. **14**: 473, 1938.
9. Robertson, H. E.: The Persistence of Tuberculous Infections, Am. J. Pathol. (supp.) **9**: 711, 1933.
10. Wallgren, A.: Pulmonary Tuberculosis: Relation of Childhood Infection to Diseases in Adults, Lancet **1**: 417, 1938.
11. Editorial: Endogenous Reinfection and Primary Complex, Am. Rev. Tuberc. **38**: 791, 1938.
12. Tortone, J., Chattas, A., Myers, J. A., Stewart, C. A., and Streukens, T.: Tuberculosis in Children Less Than Six Years of Age. (To be published in Am. J. Dis. Child.)
13. Rich, A. R.: The Influence of Age-Determined Factors on the Development of Tuberculosis, Minnesota Med. **21**: 745, 1938.
14. Myers, J. A., Streukens, T., and Ch'iu, P. T. Y.: Clinical and Epidemiological Aspects of Primary Infection in Adults, National Tuberculosis Association, p. 109, 1938.
15. Sweany, H. C.: Primary Tuberculous Infection in Adults, National Tuberculosis Association, p. 107, 1938.
16. Price, Dorothy: Tuberculosis in Infants, Brit. M. J. **1**: 275, 1938.
17. Braily, Miriam: Factors Influencing the Course of Tuberculous Infection in Young Children, Am. Rev. Tuberc. **34**: 347, 1937.

18. Ch'iu, P. T. Y., Myers, J. A., and Stewart, C. A.: The Fate of Children With Primary Tuberculosis, J. A. M. A. **112**: 1306, 1939.
19. Gruskin, B., Louria, A. A., Bennett, R. H., and Schwartz, E.: An Intradermal Test for the Determination of Active Tuberculosis, Dis. of Chest. **4**: 22, 1938.
20. Seibert, F. B.: The Relationship Between the Sensitizing Properties of Tuberculoprotein and Its Molecular Weight, Tr. Nat. Tuberc. A. **29**: 165, 1933.
21. Nelson, W. E., Mitchell, A. G., and Brown, E. W.: The Possibility of Sensitization to Tuberculin, Am. Rev. Tuberc. **37**: 286, 1938; J. PEDIAT. **12**: 26, 1938.
22. Lincoln, E. M., Raia, A., and Gilbert, L. A.: Tuberculin Reactions in Children, J. PEDIAT. **12**: 479, 1938.
23. Crimm, P. D., Short, D. M., and Wood, H. E.: Qualitative and Quantitative Evaluation of Old Tuberculin and Purified Protein Derivative (P.P.D.) With X-ray Correlation on 1,003 Children, Tr. Nat. Tuberc. A. **33**: 139, 1937.
24. Vollmer, H., and Goldberger, E. W.: A New Tuberculin Patch Test, Am. J. Dis. Child. **54**: 1019, 1937.
25. Idem: Comparative Study of the Tuberculin Patch Test and the Mantoux Intracutaneous Test, Am. J. Dis. Child. **56**: 584, 1938.
26. Steele, A. H., and Willis, H. S.: The Application of the Newer Purified Tuberculin Products by the Pirquet Method, Am. Rev. Tuberc. **36**: 309, 1937.
27. Paretzky, M.: The Diagnostic Application of High Doses of Tuberculin, Am. Rev. Tuberc. **36**: 313, 1937.
28. Howe, J. S.: Daily Variations in Tuberculin Reactions: Their Relation to the Vascular Pressor Episode, Tr. Nat. Tuberc. A. **33**: 139, 1937.
29. Stewart, C. A.: Periodic Accrediting of Households, Am. J. Dis. Child. **54**: 699, 1937.

704 EQUITABLE BUILDING

American Academy of Pediatrics

Proceedings

EIGHTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

DEL MONTE, CALIF., JUNE 10 AND 11, 1938

Round Table Discussion of the Teaching of Body Mechanics in Pediatric Practice

Chairman, Dr. Clifford Sweet, Oakland, Calif.
Assistant, Dr. Herbert E. Coe, Seattle, Wash.

CHAIRMAN SWEET.—A clear understanding of the mechanics of the human body in rest and in motion must rest on certain fundamentals:

1. The body is subject to the laws of gravity, and maintenance of good posture with the least muscular effort demands that the body be arranged, as nearly as possible, symmetrically about a vertical line passing through the body's center of gravity. In other words, to maintain the upright posture each part of the body must be counterbalanced by another part with an equal moment of force (moment of force: mass × horizontal distance from the center of rotation) or by muscular contraction sufficient to balance the inequality. This indicates clearly that, when for any reason some part of the body is extended too far from the center of gravity in a horizontal direction, another part will be extended too far in the opposite horizontal direction to restore balance, adjusted by the semicircular canals to maintain the visual plane parallel to the earth's surface.

2. All skeletal muscles are arranged in pairs as antagonists: for every flexor there is a corresponding extensor. These antagonistic muscles are at rest only when they are simultaneously relaxed, which is possible only when the part which they move or support is in equilibrium. Any muscle which has the linear distance between its origin and insertion shortened takes up the slack thus allowed and increases both in cross section and strength, while any increase in length or stretching produces a corresponding decrease in strength, with a corresponding decrease in cross section. In general the strength of a muscle varies directly with its cross section and indirectly with its length. Any advantage which a muscle gains over its opponent increases steadily—the strong muscle gains and the weak muscle loses strength—thereby increasing the departure from equilibrium, with the production of increasing deformity. Certain muscles, because of their great strength and because they are shortened when the body is in a habitual incomplete upright posture, in a long-continued sitting posture, especially if slumping is added, or in an incorrect lying posture, are most frequently able to gain and increase their advantage over their opponents. In general, those are the muscles which were of greatest use when our ancestors traveled on all fours and those which must exert the most force in maintaining the active equilibrium of the body in the present upright posture. The psoas and pectoral muscles are an example of the first group and the gastrocnemius of the second.

3. All deformities, with the exception of those apparent ones which represent a stage of development in the growing child, tend to increase. The reasons for this increase are as follows: The deformity allows the shortening and therefore the gain in strength of muscles over their opponents; growth takes place in the direction of use (Wolff's law); any posture or method of movement tends to become implanted in the kinesthetic sense as a habit; generally it is easier and more comfortable to rest and move with a deformity than against it toward correction, and in the young, growing child with his elastic tissues and his great skill for learning new, substitute stances and movements, deformities, even though considerable, rarely cause sufficient discomfort to make their correction mandatory.

4. Ontogeny recapitulates phylogeny in the development of body mechanics as truly as in other aspects of growth and development. Every child must learn to sit up, to stand upright, and to walk and run as a biped. His level of skill may stop at any of the stages leading toward perfection in these skills as truly as it may in music or mathematics. Beethoven's Fifth Symphony is not for beginners, and higher mathematics does not yield to the multiplication tables alone.

As in all other development of the human being, heredity and environment have the principal roles. Heredity determines the quality of the body with which he begins life and the energy or "spirit" which will give him the urge "to strive forward toward perfection in all things," while environment contributes the conditions which will aid him in his upward struggle or place obstacles in his path. The ideal environment is that which enables him to make the most of his hereditary possibilities. Skill in standing, walking, running, sitting, and relaxation, all of which are so useful in everyday living and a lack of which allows so much injury to the body, surely is of sufficient importance to warrant one's best efforts as teachers of parents and children.

Six cases were presented demonstrating varying postural defects.

Dr. Coe in discussing the first case stated that the shortening of the hamstring muscles keeps pelvis rotated improperly, that the short posterior group may be due to ballet dancing which prevented proper dorsiflexion. Exercises and not Thomas heels are needed to correct this condition.

DR. WILLIAM WESTON (COLUMBIA, S. C.).—Do you find that children who do toe dancing exaggerate the sway back and failure of flexion?

CHAIRMAN SWEET.—Yes, but I have no objection to walking on toes.

Dr. Coe in presenting second case emphasized the fact that this boy, aged 12 years, presented a pelvis rotated forward, with increased lumbar lordosis and mild hyperextension of knees, and suggested, as an exercise for short heel cords, that the patient kneel slightly with feet on floor and feet parallel.

DR. G. M. CULTRA (AMARILLO, TEXAS).—What do you think of having child lying down with knees flexed and then trying to sit up?

CHAIRMAN SWEET.—The rectus muscles do not have much to do with posture. I am more interested in the oblique abdominals. I feel that the recti will take care of themselves. I divide the body into two kinds of structures, those that support weight and the others that are carried about as passengers. I cannot walk or work with chest up and rectus tight; it is not natural to hold abdomen in uncomfortably.

DR. W. A. MCGEE (RICHMOND, VA.).—How often do you advise exercises?

CHAIRMAN SWEET.—Five minutes night and morning and a mattress that supports the body horizontally during sleep.

DR. H. R. LUSIGNAN (MONTEREY, CALIF.).—Would toe dancing be contraindicated?

CHAIRMAN SWEET.—No, but I would give foot exercises and recommend walking pigeon-toed; our job is to keep the feet strong and balanced.

DR. G. B. KRYDER (Los Angeles).—What are the contraindications to going barefoot?

CHAIRMAN SWEET.—None, except rattlesnakes; give the children freedom and an opportunity to use their feet.

DR. KRYDER.—What about Keds?

CHAIRMAN SWEET.—Keds, if ventilated, are good.

DR. KRYDER.—I had a patient who used Keds for jumping; he awoke each morning with pains in his feet, but on changing to shoes with heel this disappeared.

CHAIRMAN SWEET.—High jumpers use a heeled track shoe. I formerly thought that Keds were detrimental, but now I do not feel so about them. A corn on the little toe indicates that the shoe does not fit snugly in the heel.

DR. KRYDER.—At what age do you begin exercises?

CHAIRMAN SWEET.—This is covered in the charts. If the child has a very weak foot put on heel shoe at about 15 months.

DR. EDITH BOYD (Minneapolis, Minn.).—Why wear heel at all?

CHAIRMAN SWEET.—Because it is easier to balance on the center of gravity if one wears heels. The tendency for most people is to drop back on the heels.

DR. McGEE.—Do you like the moccasin shoe?

CHAIRMAN SWEET.—Yes, I do.

GUEST IN AUDIENCE.—What is wrong with a shoe that causes a bunion to develop?

CHAIRMAN SWEET.—Too short a shoe. Avoid rigid soled shoes or too short shoes from the onset.

DR. E. G. SCHWARZ (Fort Worth, Texas).—What do you think of Taylor Tots or other devices as causative factors?

CHAIRMAN SWEET.—I do not feel that a child stays in a walker long enough to do any harm. I think that brings up a problem of child psychology. I am trying to teach mothers to keep the child sheltered and protected while he is busy, but later to devote considerable pleasant attention to the child.

MRS. OSCAR REISS (Los Angeles, Calif.).—With preschool child is it necessary to fit the chair to the child?

CHAIRMAN SWEET.—I feel that to keep a child in a chair that is too large for him is bad; otherwise not, if there is only a slight variation.

DR. LANGLEY PORTER (San Francisco).—Give a child activities that teach him to reach above his head; this will give strength to upper trunk. I feel that the barefoot child has a strengthened foot and that slow walking is frequently due to heavy bedclothes, causing foot drop.

CHAIRMAN SWEET.—I dislike all shoes with corrections early in life; I have no objection to a little lift at the heel, not in the sole. I feel that a shoe should not interfere with the flexion of the foot.

DR. LUSIGNAN.—Does not the Thomas heel make children grasp with the toes?

CHAIRMAN SWEET.—Yes, I think it does to a certain extent. However, if the foot is in a shoe with a rigid shank and rigid sole, not much can be done in the way of grasping.

DR. LUSIGNAN.—Why do obstetricians advise mothers to wear low broad heels?

CHAIRMAN SWEET.—I think to increase the stability primarily, particularly in walking. If the expectant mother is taught to stretch her posterior leg muscles, she can wear the low broad heel comfortably and with permanent advantage.

DR. E. J. BARNETT (SPOKANE, WASH.).—Would you like to say what brand of shoes you would prefer for young children?

CHAIRMAN SWEET.—I do not wish to advertise any particular brand of shoe. There are several excellent makes of shoes, many of which I am not acquainted with. My minimum requirements for a shoe are that it be made on a combination last, since all children have combination feet; that it be sufficiently flexible for the child to walk in it easily; and that it fit the child's foot.

DR. JACOB WALLEN (PHILADELPHIA).—How about shoes for infants who are just learning to walk?

CHAIRMAN SWEET.—I prefer to have children who are just learning to walk go barefooted at least part of the time. When shoes are worn, I think they should be flexible, of the soft moccasin type.

DR. LUSIGNAN.—Do you ever attempt to keep the heavy child from early weight-bearing by using a walker?

CHAIRMAN SWEET.—I have not attempted to prevent weight-bearing by the use of a walker. I think, in general, one may quite safely let the child follow any activity which his own abilities can support.

DR. J. R. LEMMON (AMARILLO, TEXAS).—Will you say something about the bandy-legged child and what corrective measures you would advise?

CHAIRMAN SWEET.—Any child who has any deformity should first be carefully examined. For example, Dr. Lemmon, the type of child you refer to may have calf muscles that are too long and need heeled shoes. He may have weak or poorly developed abdominal muscles, or he may need particular attention to his gluteal muscles in order to strengthen and develop the external rotators of the femurs.

DR. N. L. MOORE (SANTA ANNA, CALIF.).—Do sleeping posture and the type of mattress play a part?

CHAIRMAN SWEET.—Sleeping posture and the type of mattress do play a part in the development of children. A mattress should be firm and should be supported in a horizontal manner either by efficient springs that are tied together diagonally or by boards placed between the spring and the mattress.

DR. HUGHES KENNEDY, JR. (BIRMINGHAM, ALA.).—Can you get a 4-year-old child to cooperate with exercises. I have in mind a child with flat feet and leg pain.

CHAIRMAN SWEET.—Yes, I think a 4-year-old child will cooperate with exercises, provided that they are presented in the form of a game. For example a child will raise himself from the prone to the sitting position, thereby using the abdominal muscles many times, provided that someone does it with him and calls it a game. The child you describe with leg pains should be checked over to see whether or not he has abnormally long or short muscles.

DR. EDWIN G. SCHWARZ, Secretary
Fort Worth, Texas

News and Notes

The committee in charge of the **Fifth International Congress of Pediatrics,** which will convene in Boston and Cambridge, Mass., Sept. 2, 3, 4, and 5, 1940, announces the following tentative program:

Monday, September 2—

Registration.
Business Meeting of National Committees of Congress.

Tuesday, September 3—

Harvard University, Cambridge, Mass.
A.M. Referat: Deficiencies of the Vitamin B Complex.
P.M. Discussion—4 selected subjects.

Wednesday, September 4—

Harvard Medical School, Boston, Mass.
A.M. Sectional meetings.
P.M. Scientific exhibits, excursions, and sports.

Thursday, September 5—

Harvard University, Cambridge, Mass.
A.M. Discussion—4 selected subjects.
P.M. Referat: Viruses in Relation to Disease in Infancy and Childhood.
Evening—Banquet.

Representative pediatricians from various countries will participate in the referats and discussions at the general assemblies. Individuals desiring to submit papers either for the general or sectional meetings should do so through the national committee of the country they represent. Each title sent by the various national committees to the general secretary must be accompanied by an abstract not in excess of 300 words of the material to be presented.

There will be four official languages for the Congress, English, French, German and Italian. The choice of these languages in which the papers may be presented will be left to the discretion of the essayist. At the general sessions of the Congress a translation system will be installed with earphones at each seat. While the speaker is presenting his data, translators will repeat what he says in the other Congress languages so that the listener may hear the speech in any one of these languages which he prefers.

Arrangements are being made for scientific exhibits and for excursions to points of medical interest in and about the city; while the women's committee are making special arrangements for the entertainment of women members of the Congress as well as for the wives of the participating members.

INDEX TO VOLUME 14

A

Abnormality, congenital, of aorta, constricting double arch of, in infancy, 527
of heart: mental retardation associated with, 21
of intestine in infant, 115

Acrodynia, treated with intramuscular injections of vitamin B_6, 74

Adolescence, period of, 276 (book review)

Agranulocytosis, experimental, 116

Aikman, John, 113

Air, mold spore content of, in Boston, 234

Allen, Willard M., 115

Allergic diseases, 92 (critical review)

American Academy of Pediatrics, eighth annual meeting, 118, 255, 385, 395, 534, 832
executive board's meeting, 251
news, 134, 274, 414, 556, 693
Region I meeting, 105
state chairmen's meeting, Region III, 117

Amyotonia congenita, three cases of, 114

Anderson, W. A. D., 375

Androgen, treatment of cryptorchidism with, 452

Anemia, Cooley's, 349
erythroblastic, in adolescent, 349
Mediterranean, 349
of rheumatic fever, 66
sickle-cell, cerebral vascular lesions accompanying, 745

Angioma, congenital, diagnosis and treatment, 671

Antigen, undenatured bacterial, comparison of phase I, *H. pertussis* vaccine with, 25

Antitoxin, staphylococcal, case of severe staphylococcal infection treated with, 114

Aorta, congenital abnormality of, constricting double arch of, in infancy, 527

Arena, J. M., 745

Artery, pulmonary, in Ayerza's disease, 602

Ascorbic acid (*see* Vitamin C)

Asthma, infectional, treatment of, in children, with filtrate of cultures of upper respiratory pathogenic bacteria, 307

Atropine intoxication, 755

Ayerza's disease (*see* Artery, pulmonary)

B

B. alkalescens in stool of normal infant, 341

Baker, Charles J., 183

Bakwin, Harry, 1
— and Jacobziner, H., 730

Barbour, G. M., Carpenter, C. M., and Hawley, P. L., 116

Basman, Jack, and Zentay, P. J., 323

Baum, W. S., and McCoord, A. B., 110

Berkley, Hugh K., 79

Bernstein, Samuel S., Williams, H. H., Hummel, F. C., Shepherd, M. L., and Erickson, B. N., 570

Bile duct, common, idiopathic dilatation of, in childhood, 79

Biophotometer, visual adaptation as tested with, and vitamin A content of blood, 110

Birth, blood studies of vitamin C during pregnancy, and early infancy, 447

Birthmark (*see* Tumors, angioma)

Black, William C., 761

Blatt, Maurice L., and Wolf, A. A., 695

Blood collections, needle guide and apparatus for, 383
fats of, increased essential, metabolic observations on child with, 570
parental whole, treatment of measles with, 502
pressure, determination of, in children, 148
vessels, cerebral, lesions of, accompanying sickle-cell anemia, 745

Body mechanics, teaching of, in pediatric practice, 832 (round table discussion)

Book reviews, 276, 415, 558

Boston, air of, mold spore content of, 234

Bradford, W. L., and Wold, M., 114
Breese, B. B., 110
Bronchiectasis, acute, abscess from, simulating empyema, 661
tuberculous atelectatic, 368
Bronchiolectasis, congenital familial steatorrhea with fibromatosis of pancreas and, 462
Bronchography in children, 780
Bronstein, I. P., 203
Burgess, Ernest, Durand, J. I., and Spickard, V. W., 74
Bush, Fred W., 113
Butter fat, oils as substitutes for, in infant feeding, 290

C

Calcification, renal, in infancy and childhood, 375
Carcinoma, congenital, of thymus with extensive generalized metastases, 798
primary, of liver, in six-year-old girl, 113
Card, Thomas A., 658
Caries, dental, significance of, as an indication of nutritional adjustment, 118 (round table discussion)
Carnes, Moses, Kanof, A., and Kramer, B., 712
Carpenter, C. M., Barbour, G. M., and Hawley, P. L., 116
Catheter, buccal oxygen-ether, 807
Celiac disease, congenital familial, with fibromatosis of pancreas and bronchiolectasis, 462
vitamin absorption tests in, and nonceliac disease, 110
Cerebral sclerosis, familial (Pelizaeus-Merzbacher type), 113
Child, Weil's disease occurring in, 48
Childhood, idiopathic dilatation of common bile duct in, 79
kidney, calcification of, in infancy and, 375
Children, adolescent, 276 (book review)
asthma, infectional, treatment of, in, with filtrates of cultures of upper respiratory pathogenic bacteria, 307
blood pressure, determination in, 148
bronchography in, 780
disorders of gonad function in, 242
empyema in, 11
encephalitis, epidemic type B in, 323
hypergenitalism in, 203
prognosis of chronic glomerular nephritis in, 111
repeated glucose tolerance tests in, 737
Children—Cont'd
tuberculosis in, 815 (critical review)
tularemia in, 358
tumors, neurogenic, of sympathetic nervous system in, 137
Christie, Amos U., Dunham, E. C., and Jenss, R. M., 156
Circulation, moving picture demonstration of, within mesentery of rabbit, 115
Clausen, S. W., 110
Clifford, Stewart H., 333
Cohen, Robert, 383, 807
Comments, 136, 416
Convulsions, factors influencing relation of, and hyperthermia, 190
Correspondence, 691
Critical review:
allergic diseases, 92
disorder of gonad function in children, 242
modifiability of growth by administration of endocrine substances, 684
tuberculosis in children, 815
Crook, Grace W., Winters, M., and Tompkins, C. A., 788
Cryptorchidism, treatment of, with gonadotropic substance, 452

D

Davison, Wilburt C., 810
Day, Richard, 148
Deaf, congenitally, phenylketonuria and, 348
Dermatorrhexis (Ehlers-Danlos syndrome), 632
Development, child, biographies of, 558 (book review)
consideration of race and sex in relation to growth and, of infants, 156
precocious somatic and sexual, in infant, 113
Diarrhea, epidemic, in newborn, 183
Dunham, Ethel C., Jenss, R. M., and Christie, A. U., 156
Duodenitis, acute infectious, 213
Durand, Jay I., Spickard, V. W., and Burgess, E., 74
Dysentery, bacillary, treatment of, in infants and children, with pectin-agar diet, 788

E

Ehlers-Danlos syndrome (*see* Skin, abnormalities)
Emphysema, subcutaneous, in newborn infant, 805

Empyema, acute bronchiectatic abscesses simulating, 661
in children, 11
Encephalitis, type B epidemic, in children, 323
Epstein, J. W., and Wasserman, P., 798
Erickson, Betty Nims, Bernstein, S. S., Williams, H. H., Hummel, E. C., and Shepherd, M. L., 570

F

Fever, vitamin A content of blood in, 110
Field, Elsie H., and Gillespie, J. B., 363
Fischer, Alfred E., Kohn, J. L., and Resch, H. V., 502
Fluoroscopy, device to aid in, of infant, 382
Fries, Joseph Harman, 382
Frontali, G., 290
Fulton, Robert P., Toomey, J. A., and Rea, F. W., 372
Fungi, spores of, content of air in Boston, 234

G

Gachet, Frederick S., 111
Geib, Fred W., 116
Gerbasi, Michael J., 113
Gerber, Alexander, and Stein, J. L., 89
Gershon-Cohen, J., Thalheimer, E. J., and Mezzetti, A., 349
Gillespie, James B., and Field, E. H., 363
Girls, adolescent, physical strength of, 610
Glaser, Jerome, 114
Glucose tolerance, repeated tests for, in children, 737
Gonad, function of, disorders of, in children, 242
Gonadotropic substance (*see* Androgen)
Greenwald, Harry M., and Wasch, M. G., 57
"Growing pains," nonrheumatic, differential diagnosis of, and subacute rheumatic fever, 315
Growth, consideration of race and sex in relation to, and development of infant, 156
modifiability of, by administration of endocrine substances, 684 (critical review)
Grulee, Clifford G., Sanford, H. N., and Lewison, M., 725
Guillain-Barré syndrome, 363

H

H. pertussis, experimental infection in mouse produced by intranasal inoculation with, 114
Hahn, Paul F., 112
Hamilton, Bengt, 517
Hamilton, Paul M., and Togasaki, Y., 655
Harvey, Roger, and Warren, S. L., 115
Hawley, Estelle, and Kaiser, A. D., 116
Hawley, P. L., Carpenter, C. M., and Barbour, G. M., 116
Head injuries in children, 116
Heart disease, congenital, mental retardations associated with, 21
Hemangioma, congenital, in infancy, diagnosis and treatment, 115
Hematoma, calcified, 522
Hemorrhagic disease of newborn (*see* Infant, newborn, hemorrhage in)
Heredity, role of, in stuttering, 642
Hill, Lee Forest, and Kelly, D. H., 815
Hodes, Horace L., Stifler, W. C., Jr., Walker, E., McCarty, M., and Shirley, R. G., 417
Howard, P. J., 220
Hubbard, John P., and McKee, M. H., 66
Hummel, Francis C., Bernstein, S. S., Williams, H. H., Shepherd, M. L., and Erickson, B. N., 570
Hurwitz, Samuel, and Stephens, H. B., 11
Hyland, Clarence M., 255
Hypergenitalism in children, 203
Hyperlipemia, essential, 570
Hyperthermia, factors influencing relation of convulsions and, 190
Hypoparathyroidism, physiologic, and tetany in newborn, 1

I

Infancy, early, blood studies of vitamin C during pregnancy, birth and, 447
kidney, calcification of, in childhood and, 375
syndrome of constricting double aortic arch in, 527
Infant, feeding of, oils as substitutes for butter fat in, 290
fluoroscopy of, device to aid in, 382
food for, irradiated evaporated milk as, 725
growth and development of, consideration of race and sex in relation to, 156

Infant—Cont'd
newborn, epidemic diarrhea in, 183
hemorrhage in, 333
sepsis of, 695
subcutaneous emphysema in, 805
tetany in, relation to physiologic hypoparathyroidism, 1
normal, *B. alkalescens* in stools of, 341
prevention of purulent otitis media in, 730
Ingalls, Theodore Hunt, 593
Inoculation, intranasal, experimental infection in mouse produced by, with *H. pertussis*, 114
Iron, absorption and excretion of, in normal and anemic dogs under experimental conditions, 112

J

Jackson, S. H., and Snelling, C. E., 447
Jacobziner, Harold, and Bakwin, H., 730
Jaundice, infectious, 213
spirochetal, occurring in child, 48
Jenss, Rachel M., Dunham, E. C., and Christie, A. U., 156
John, Henry J., 737
Jones, T. Banford, 115

K

Kaiser, Albert D., and Hawley, E., 116
Kanof, Abram, Kramer, B., and Carnes, M., 712
Kelly, Dennis H., and Hill, L. F., 815
Kenney, Athol S., and Rapoport, M., 161
Kidney, calcification of, in infancy and childhood, 375
Kohn, Jerome L., Fischer, A. E., and Resch, H. V., 502
Kramer, Benjamin, Kanof, A., and Carnes, M., 712
— and Merksamer, D., 51

L

Larcomb, John W., 348
Lawrence, John S., 116
Leslie, Charles J., and de Sanctis, A. G., 83
Lester, Charles W., and Rovenstine, E. A., 780
Leucemia, experimental, some aspects of, 112
Levinson, Samuel A., 506
Lewis, J. M., 559
Lewison, Matthew, Grulee, C. G., and Sanford, H. N., 725
Lichty, John, and MacColl, W. A., 114
Lipoidosis, Niemann-Pick's disease, phosphatid, three cases in one family, 51
Litvak, Abraham M., Rauch, S., and Steiner, M., 462
Lymphosarcoma, pleomorphous cell, of thymus, 618

M

Martmer, Edgar E., 48
MacColl, William A., 277
— and Lichty, J., 114
McCarty, Maclyn, Hodes, H. L., Stifler, W. C., Jr., Walker, E., and Shirley, R. G., 417
McCoord, Augusta B., 111
— and Baum, W. S., 110
McDonald, J. J., and Sauer, L. W., 304
McKee, Margaret Harper, and Hubbard, J. P., 66
McMann, Walter, and Purcell, C. W., 805
Measles, early, treatment of, with parental whole blood, 502
pneumonia, pneumococcic, associated with, use of sulfapyridine in primary pneumococcic pneumonia and in, 417
Medicine in modern society, 558 (book review)
Meningitis, meningococcic, serum treatment of, 83
tuberculous, tryptophan bodies in, 372
Menstrual difficulties, early adolescent, 115
Mental tests, retardation associated with congenital heart disease, 21
Merksamer, David, and Kramer, B., 51
Mezzetti, Alfred, Thalheimer, E. J., and Gershon-Cohen, J., 349
Mider, G., Burroughs, and Morton, J. J., 112
Milk, irradiated evaporated, as food for infants, 725
Mold (*see* Fungi)
Morton, Henry G., 755
Morton, John J., and Mider, G. B., 112

N

Needle, guide for, and blood collection apparatus, 383
Nelson, Richard L., 39
Nelson, Severina E., 642

Nephritis, chronic, prognosis of, value of urea clearance tests in, 111
glomerular, chronic, prognosis of, in children, 111
Nerves (Guillain-Barré syndrome), acute polyneuritis of uncertain origin, 363
Neuritis, multiple acute, of uncertain origin (Guillain-Barré syndrome), 363
Neustadt, Adolph, and Weiner, S. B., 752
News and notes, 135, 275, 414, 557, 694, 836
Niemann-Pick's disease (*see* Lipoidosis)
Noyes, Harold J., 118
Nursery, adoption, aseptically conducted, midsummer respiratory infection in an, 304
Nutrition, adjustment of, dental caries as indication of, 118 (round table discussion)
newer diagnostic methods, 415 (book review)

O

Oils, substitutes for butter fat in infant feeding, 290
Omphalocele, congenital, 89
Otitis media, purulent, prevention of, in infants, 730

P

Paige, Beryl H., and Wright, F. H., 137
Pancreas, fibromatosis of, congenital familial steatorrhea with, and bronchiolectasis, 462
Panel discussion, thymus gland, 534
Parathyroidism, physiologic hypo-, relation of, to tetany in newborn infants, 1
Pectin-agar diet, in treatment of bacillary dysentery of infants and children, 788
Pediatrics, American, future of, 810
practice of, teaching of body mechanics in, 832 (round table discussion)
school health problem and relation to, 385 (round table discussion)
Pelizaeus-Merzbacher type of cerebral sclerosis, 113
Pericarditis of unrecognized etiology, 112
Pertussis (*see* Whooping cough)
Phenylketonuria and congenitally deaf, 348
Physical strength of adolescent girls, 610
Pneumonia, pneumococcic, associated with measles, use of sulfapyridine in primary pneumococcic pneumonia and in, 417
primary, use of sulfapyridine in, and in pneumococcic pneumonia associated with measles, 417
saw-tooth form, 517
staphylococcus, clinical, pathologic and bacteriologic study of, 712
Polyneuritis, acute, of uncertain origin, 363
Posson, Donald D., 114
Pratt, Henry N., 234
Pregnancy, blood studies of vitamin C during birth and early infancy and, 447
Pryor, Helen Brenton, and Smith, R. T., 610
Purcell, C. W., and McMann, W., 805
Pyloric stenosis, hypertrophic, in twins, 658

R

Race and sex, consideration of, in relation to growth and development of infants, 156
Rapoport, Milton, and Kenney, A. S., 161
Rauch, Solomon, Litvak, A. M., and Steiner, M., 462
Rea, Frederick W., Toomey, J. A., and Fulton, R. P., 372
Resch, Henry Ulmer, Kohn, J. L., and Fischer, A. E., 502
Respiratory system infection, midsummer, in aseptically conducted adoption nursery, 304
Reynold, Edwin R., 112
Rheumatic fever, 395 (round table discussion)
acute, 581
anemia of, 66
subacute, differential diagnosis of nonrheumatic "growing pains" and, 315
vitamin C studies in, in children, 116
Rickets, treatment of tetany and, with single massive dose of vitamin D, 491
Riesman, David, 558
Roentgenologic demonstration of esophageal varices as diagnostic aid in chronic thrombosis of splenic vein, 57

Rogatz, Julian L., 618
Ross, Mabel, 21
Round table discussions:
convalescent serum therapy, 255
dental caries—the disease and its significance as an indication of nutritional adjustment, 118
rheumatic fever, 395
school health problems and relation to pediatrics, 385
teaching of body mechanics in pediatric practice, 832
Rovenstine, E. A., and Lester, C. W., 780

S

de Sanctis, Adolph G., and Leslie, C. J., 83
Sanford, Heyworth N., Grulee, C. G., and Lewison, M., 725
Sauer, L. W., and McDonald, J. J., 304
Scarlet fever, complications of, prophylaxis of, 655
School health problems, relation to pediatrics, 385 (round table discussion)
Sclerosis, tuberous, 113
Scurvy, infantile, 593
prophylaxis and treatment of, use of crystalline vitamin C (ascorbic acid) in, and some other disorders of infancy and childhood, 161
Septicemia of newborn infant, 695
Serum therapy, convalescent, 255 (round table discussion)
Sex, consideration of race and, in relation to growth and development of infant, 156
Shapiro, M. J., 315
Shaw, Robert R., 661
Shepherd, Marion L., Bernstein, S. S., Williams, H. H., Hummel, F. C., and Erickson, B. N., 570
Shirley, Robert G., Hodes, H. L., Stifler, W. C., Jr., Walker, E., and McCarty, M., 417
Siblings (*see* Children)
Singer-Brooks, Charlotte H., 25
Skin, abnormalities (Ehlers-Danlos syndrome), 632
Slesinger, H. A., and Zeligman, I., 213
Smallpox (virus), cultures of, studies relating to value of vaccination with, 114
Smith, Carl H., 632
Smith, Earl E., 602
Smith, Ruth Tangier, and Pryor, H. B., 610
Smyth, Francis Scott, 92
Snelling, Charles E., and Jackson, S. H., 447
Snoke, Albert W., 111
Snyder, Marshall L., 341
Spickard, V. W., Durand, J. I., and Burgess, E., 74
Staphylococcus infection, severe, case treated with staphylococcal antitoxin, 114
toxin, inactivation of, in vitro by sulfanilamide, 116
Steatorrhea (*see* Celiac disease)
Stein, Jacob L., and Gerber, A., 89
Steiner, Matthew, Rauch, S., and Litvak, A. M., 462
Stephens, H. Brodie, and Hurwitz, S., 11
Stevens, Franklin A., 307
Stifler, William C., Jr., Hodes, H. L., Walker, E., McCarty, M., and Shirley, R. G., 417
Stools, *B. alkalescens* in, of normal infants, 341
Strong, Robert A., and Weitz, F., 522
Stuttering, role of heredity in, 642
Sulfanilamide, inactivation of staphylococcal toxin in vitro by, 116
Sulfapyridine, clinical experience with, 277
use of, in primary pneumococcic pneumonia, and in pneumococcic pneumonia associated with measles, 417
Suprarenal gland hemorrhage (Waterhouse-Friderichsen syndrome), 506
Sympathetic nervous system, neurogenic tumors of, in children, 137
Syphilis, congenital, diagnosis of, 761
ten-year study, 220

T

Talbot, Fritz B., and Talbot, N. B., 242
Talbot, Nathan B., and Talbot, F. B., 242
Taussig, Helen B., 581
Tetany, in newborn infants, relation to hypoparathyroidism, physiologic, 1
treatment of rickets and, with single massive dose of vitamin D, 491
Thalheimer, E. J., Mezzetti, A., and Gershon-Cohen, J., 349

Thymus, congenital carcinoma of, with extensive generalized metastases, 798
gland, 534 (panel discussion)
Togasaki, Yoshiye, and Hamilton, P. M., 655
Tompkins, Charles A., Winters, M., and Crook, G. W., 788
Toomey, John A., Fulton, R. P., and Rea, F. W., 372
Treatment, serum, of meningococcic meningitis, 83
Tryptophan bodies in tuberculous meningitis, 372
Tuberculin patch test, 752
Tuberculosis in children, 815
Tularemia in siblings, 358
Tumors, angioma, congenital, diagnosis and treatment, 671
carcinoma, congenital, of thymus with extensive generalized metastases, 798
hemangioma, congenital, in infancy, diagnosis and treatment, 115
lymphosarcoma, pleomorphous cell, of thymus, 618
neurogenic, of sympathetic nervous system in children, 137
primary, of liver in six-year-old girl, 113
Twins, hypertrophic pyloric stenosis in, 658

U

Urea clearance test, value of, in prognosis of chronic nephritis, 111

V

Vaccination, smallpox, value of, studies relating to, with culture virus, 114
Vaccine, phase I, *H. pertussis*, comparison of, with undenatured bacterial antigen, 25
Varices, esophageal, roentgenologic demonstration of, as diagnostic aid in chronic thrombosis of splenic vein, 57
Vein, splenic, chronic thrombosis of, roentgenologic demonstration of esophageal varices as diagnostic aid in, 57
Vision, adaptation of, as tested with biophotometer, and vitamin A content of blood, 110
Vitamin A absorption tests in celiac and nonceliac disease, 110
Vitamin A—Cont'd
content of blood in fever, 110
visual adaptation as tested with biophotometer and, 110
distribution of, in body tissues of experimental animals, 111
B_1, intramuscular injections of, acrodynia treated with, 74
C, blood studies of, during pregnancy, birth, and early infancy, 447
concentration of, in tissues in infantile scurvy, 593
crystalline, use of, in prophylaxis and treatment of infantile scurvy and some other disorders of infancy and childhood, 161
studies of, in rheumatic fever in children, 116
D, dose, single massive, in treatment of rickets and tetany, 491
effectiveness of, influence of menstruum on, obtained from livers of percomorphi order of fish, 559
shock therapy, 491
Vollmer, Hermann, 491

W

Waddell, W. W., Jr., and Wray, W. S., 358
Walker, Ethel, Hodes, H. L., Stifler, W. C., Jr., McCarty, M., and Shirley, R. G., 417
Warren, Stafford L., and Harvey, R., 115
Wasch, Milton G., and Greenwald, H. M., 57
Wasserman, P., and Epstein, J. W., 798
Waterhouse-Friderichsen syndrome (*see* Suprarenal, hemorrhage)
Webster, Bruce, 684
Wegman, Myron E., 190
Weil's disease (*see* Jaundice, spirochetal)
Weiner, Samuel B., and Neustadt, A., 752
Weitz, Frank, and Strong, R. A., 522
Whooping cough, encephalitis in, 39
neurologic complications of, 39
prophylaxis of, controlled study of: comparison of phase I, *H. pertussis* vaccine with undenatured bacterial antigen, 25
Williams, Harold H., Bernstein, S. S., Hummel, F. C., Shepherd, M. L., and Erickson, B. N., 570
Wilson, Reginald, 368

Winters, Matthew, Tompkins, C. A., and Crook, G. W., 788
Wold, Mary, and Bradford, W. L., 114
Wolf, A. Alvin, and Blatt, M. L., 695
Wolin, David, 113
Wolman, Irving J., 527
Wray, W. S., and Waddell, W. W., Jr., 358
Wright, F. Howell, and Paige, B. H., 137

Y

Young, Forrest, 115, 671

Z

Zeligman, I., and Slesinger, H. A., 213
Zelson, Carl, 452
Zentay, Paul J., and Basman, J., 323

INDEX NUMBER

Vol. 14 JUNE, 1939 Hospital Library No. 6

THE JOURNAL OF PEDIATRICS

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The Journal of Pediatrics

CONTENTS FOR JUNE, 1939

Original Communications

Sepsis of the Newborn Infant. Maurice L. Blatt, M.D., and A. Alvin Wolf, M.D., Chicago, Ill. ---- 695

Staphylococcus Pneumonia. Abram Kanof, M.D., Benjamin Kramer, M.D., and Moses Carnes, M.D., Brooklyn, N. Y. ---- 712

Irradiated Evaporated Milk as a Food for Infants. Clifford G. Grulee, M.D., Heyworth N. Sanford, M.D., and Matthew Lewison, M.D., Chicago, Ill. 725

Prevention of Purulent Otitis Media in Infants. Harry Bakwin, M.D., and Harold Jacobziner, M.D., New York, N. Y. ---- 730

Repeated Glucose Tolerance Tests in Children. Henry J. John, M.D., Cleveland, Ohio ---- 737

Cerebral Vascular Lesions Accompanying Sickle-Cell Anemia. J. M. Arena, M.D., Durham, N. C. ---- 745

Tuberculin Patch Test. Samuel B. Weiner, M.D., and Adolph Neustadt, M.D., New York, N. Y. ---- 752

Atropine Intoxication. Henry G. Morton, M.D., Durham, N. C. ---- 755

Diagnosis of Congenital Syphilis. William C. Black, M.D., San Diego, Calif. 761

Bronchography in Children. Charles W. Lester, M.D., and E. A. Rovenstine, M.D., New York, N. Y. ---- 780

Pectin-Agar Diets in the Treatment of Bacillary Dysentery of Infants and Children. Matthew Winters, M.D., Charles A. Tompkins, M.D., and Grace W. Crook, Indianapolis, Ind. ---- 788

Congenital Carcinoma of the Thymus With Extensive Generalized Metastases. P. Wasserman, M.D., Cincinnati, Ohio, and J. W. Epstein, M.D., Cleveland, Ohio ---- 798

Subcutaneous Emphysema in the Newborn Infant. Walter McMann, M.D., and C. W. Purcell, M.D., Danville, Va. ---- 805

A Buccal Oxygen-Ether Catheter. Robert Cohen, M.D., Louisville, Ky. ---- 807

The Future of American Pediatrics. Wilburt C. Davison, M.D., Durham, N. C. ---- 810

Critical Review

Tuberculosis in Children. Lee Forrest Hill, M.D., and Dennis H. Kelly, M.D., Des Moines, Iowa ---- 815

American Academy of Pediatrics

Eighth Annual Meeting of the American Academy of Pediatrics. Proceedings: Round Table Discussion of the Teaching of Body Mechanics in Pediatric Practice ---- 832

News and Notes

News and Notes ---- 836

Index

Index ---- 837

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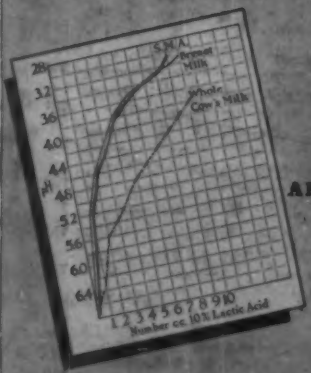

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